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CLINICAL AND BACTERIOLOGICAL STUDY OF RESECTED TUBERCULOUS PULMONARY LESIONS*

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IN ORDER TO ASSESS the scope and mode of action of present-day chemotherapy of tuberculosis, many workers[1, 3, 5, 6] in recent years have concentrated their attention upon the correlation of clinical and radiological with bacteriological and pathological data obtained from resected pulmonary lesions. When a full appreciation of these data has been gained and sufficient information has become available on the results of two large and comparable groups of patients, one treated with chemotherapy followed by excision, the other treated by chemotherapy alone or supplemented by collapse measures, it will be possible to define the position of excisional surgery in pulmonary tuberculosis.

The difficulties encountered in such a comprehensive study are obviously great. Firstly, the disease is so pleomorphic that it is almost impossible to reach uniformity in pathological classification; furthermore, a long time is necessary to evaluate late results. However, if clinicians and surgeons entrusted with the care of tuberculous patients would combine their efforts by investigating and publishing their own findings and impressions, many thousands of cases should soon be available from which to draw reliable conclusions.

We present in this study some correlation between clinical, bacteriological and radiographic changes induced by chemotherapy and corresponding pathological and bacteriological findings on resected specimens. An attempt will be made to elicit significant points which, knowing type and duration of chemotherapy, would enable one to anticipate preoperatively the pathological and bacteriological features of the resected specimen. If such criteria emerge from this or similar studies, it should be possible to decide on a more solid basis whether certain cases should be operated on or treated by chemotherapy and rest alone.

MATERIAL AND CLASSIFICATION

One hundred and sixty-two pulmonary resections performed in our service at the Saskatoon Sanatorium between October 1952 and December 1954 were analysed. The criteria of acceptance were:

1. Complete clinical records on the case.
2. Adequate bacteriological and histological study of resected specimen.
3. Tuberculous etiology proved by histological sections.

Thirty cases failed to meet these criteria; therefore the study is based on 132 resections performed on 132 patients: pneumonectomy in 27, lobectomy in 54, segmental resection in 51.

In other similar studies, cases were classified by extent of disease, or type and duration of chemotherapy, or by closed and open lesions, or by the achievement of the "target point" of D'Esopo. We thought it simpler to classify cases by the radiographic appearance at the time of admission. With such a criterion in mind and taking into consideration the main development of the process we have grouped our lesions into four types. Classification as to type and extent is given in Table I.

Methods of study.—All operative specimens were examined by a pathologist macroscopically and microscopically. Under sterile technique the resected specimen was cut open by the surgeon, and representative areas of the major focus were obtained for smear, culture and guinea-pig inoculation. More recently with the same material egg

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TABLE I.

CLASSIFICATION AS TO TYPE AND EXTENT OF DISEASE (C.T.A.)

Type of lesion	*No. cases*	*C.T.A. classification*		
		Minimal	*Mod. advanced*	*Far advanced*
Tuberculomatous...	14	10	4	
Fibrocaseous.....	14	4	8	2
Cavitary.....	56		33	23
Destroyed lobes or lungs.....	48		7	41
Total.....	132	14	52	66

embryos have been inoculated, but this investigation is not yet completed and will be the subject of a separate report. Wherever possible, cultures in ordinary Petragnani solid medium were planted directly from the specimen; otherwise, digested material (3% sodium hydroxide) was used for both culture and guinea-pig inoculation. The inoculated animals were sacrificed after eight weeks and thoroughly examined macroscopically. The cultures were read weekly for eight weeks after planting.

TUBERCULOMATOUS LESIONS

There were 14 cases, the necrotic area ranging from 2 to 6 cm. in diameter. As shown in Table II, on admission nine cases were sputum positive and five negative. After 6-8 months of chemotherapy all positive sputum cases but one, in a diabetic, became negative, a conversion rate of 88.8%.

TABLE II.

TUBERCULOMATOUS LESIONS
SPUTUM BACTERIOLOGY BEFORE AND AFTER 6-8 MONTHS OF CHEMOTHERAPY

Sputum	*Admission*	*Preoperatively*
Positive.....	9	1
Negative.....	5	13
Total cases.....	14	Conversion rate 88.8%

As a rule streptomycin 1 g. every third day and PAS 12 g. daily were given. Radiologically the lesions had become smaller, and stable and perifocal reaction seen in early radiographs and tomograms had cleared completely at the time of operation. Resistance studies on the case which failed to convert are not available.

Bacteriological findings in resection specimens.—There were one wedge resection, eleven segmental resections and two lobectomies in this group. The 14 patients went through the operation with no mortality and no complications, either immediate or late. A follow-up of 2½ years after the first resection did not reveal any adverse effects.

As shown in Table III, 13 out of 14 cases yielded a positive smear from the resected lesion, a rate of 93%. The five cases never positive during sanatorium stay contributed four positive smears from the resected lesion.

TABLE III.

TUBERCULOMATOUS LESIONS
CORRELATION OF BACTERIOLOGY OF SPUTUM AND RESECTED LESION (6-8 Months of Chemotherapy)

Sputum	*Admission*	*Pre-operative*	*Positive lesions in resected specimens*	
			Smear	*Cult./G.P.*
Positive	9	1	9	3
Negative	5	13	4	1
Total cases 14			13 93%	4 28.5%

Positive culture or guinea-pig inoculation was obtained only in four cases, a rate of 28.5%. Three of these patients had a positive sputum on admission; one was never proved positive and had had 6 months of chemotherapy.

FIBROCASEOUS LESIONS

These were 14 in number; positive sputum on admission eleven, negative three. Most of the sputa converted between the 6th and 8th month of chemotherapy, some later, but never more than 12 months of treatment was necessary to obtain stabilization of the process (Table IV).

TABLE IV.

FIBROCASEOUS LESIONS
SPUTUM BACTERIOLOGY (6-12 MONTHS OF CHEMOTHERAPY)

Sputum	*Admission*	*Preoperatively*
Positive.....	11	0
Negative.....	3	14
Total cases.....	14	Conversion rate 100%

Clinical and radiological improvement was remarkable in all, and excision in many was advised only on the basis of previous instability or suspected activity of the fibrocaseous process.

Bacteriological findings in resected specimens.—There were ten segmental resections, two lobectomies and two pneumonectomies, with no mortality or major complications. Minor complications were, in two instances, alveolar leaks of no consequence. The late results remain very satisfactory so far. The resected specimens yielded

positive smears in all cases, even in the three who were never positive during treatment. Positive culture or guinea-pig inoculation was obtained only in three cases, a rate of 21.4% (Table V). These three patients had positive sputum on admission and twelve months of chemotherapy; two had developed partial resistance to streptomycin, one showed tuberculous bronchiectasis.

TABLE V.

FIBROCASEOUS LESIONS
CORRELATION OF BACTERIOLOGY OF SPUTUM AND OF RESECTED LESION (6-12 Months of Chemotherapy)

Sputum	*Admission*	*Pre-operative*	*Positive lesions in resected specimen*			
			Smear		*Cult./G.P.*	
Positive	11	0	11		3	
Negative	3	14	3		0	
Total cases 14			14	100%	3	21.4%

CAVITARY LESIONS

This group consists of those cases which by tomography were proved to be cavitary at some time or other before excision. By this standard we have accepted fifty-six cases, the cavities ranging from 1.5 to 9 cm. in diameter.

Preoperative chemotherapy.—This was analysed in order to correlate sputum conversion with cavity closure. Six months was the minimum period of intermittent administration of streptomycin and PAS, but later continuous prolonged courses of chemotherapy were instituted and many patients came to resection having had chemotherapy for a total of one year or more. Radiological improvement was remarkable in all cases, often absolutely dramatic, in resolving exudative lesions and in closing cavities. Drug-resistant cases were all improved except one, although a longer time was necessary to reach the desired involution. The operation was performed when the optimum stage was reached, the decision not being influenced by the persistence of cavitation or the positivity of the sputum.

Sputum bacteriology and cavity closure.—Initially sputum positive were 53, negative three. After 6-12 months of preoperative chemotherapy, 22 remained positive and 34 became negative, a conversion rate of 55.4% (Table VI). A gross correlation was attempted between sputum conversion and type and duration of chemotherapy. The conversion rate of about 55% was the maximum we could obtain, both by combining and alternating the three drugs and by prolonging their administration to one year. In more recent experience, prolonged original courses of chemotherapy have brought about a much higher conversion rate, suggesting that failure to convert the sputum nearly always means acquired drug resistance.

TABLE VI.

CAVITARY LESIONS
SPUTUM BACTERIOLOGY (6-12 MONTHS' CHEMOTHERAPY)

Sputum	*Admission*	*Preoperative*
Positive	53	22
Negative	3	34
Total cases	56	Conversion rate 55.4%

Cavity closure was assumed when the previous excavation was lost to view by tomography and definitely replaced by a corresponding fibrocaseous scar or a dense round lesion. By this standard 23 cavities closed, a rate of 41.7%, and 33 remained open (Table VII). The correspondence of the radiological diagnosis with gross pathological findings has been very close.

TABLE VII.

CAVITY CLOSURE
FOLLOWING 6-12 MONTHS' CHEMOTHERAPY
(FILLED-IN OR FIBROCASEOUS SCAR)

No. cases	*Remained open*	*Closed*	*Closure rate*
56	33	23	41.7%

A correlation between preoperative sputum findings and cavity status was established (Table VIII). It was found that preoperatively 22 sputum positive cases contributed 13 open cavities, whereas 34 negative sputum cases contributed 20 open cavities. This shows that sputum conversion does not necessarily mean cavity closure or vice versa.

TABLE VIII.

CAVITARY LESIONS
CORRELATION OF SPUTUM BACTERIOLOGY AND CAVITY STATUS FOLLOWING 6-12 MONTHS OF CHEMOTHERAPY

Preoperative sputum	*No. cases*	*Preoperative open cavity*	*Percentage*
Positive	22	13	59.9
Negative	34	20	58.8

A final correlation between bacteriology of the sputum, resistance status and cavity closure was attempted, but we can prove very little because after long-term chemotherapy one very seldom grows cultures from microscopically positive sputa.

Bacteriology in resected specimens. — There were 29 segmental resections, 25 lobectomies and two pneumonectomies. There were no major complications or deaths. Seven patients had minor non-tuberculous complications. In two, the sputum failed to convert immediately after operation, but later only one became intermittently positive and this was resistant to streptomycin

TABLE IX.

CAVITARY LESIONS
RESECTED SPECIMEN BACTERIOLOGY IN 56 CAVITARY LESIONS (6-12 MONTHS OF CHEMOTHERAPY)

No. cases	*Positive smear*		*Positive cult. or G.P.*	
56	47	84%	16	28.5%

and isoniazid before surgery. At present, with a follow-up of two and a half years, all patients are well and sputum negative. In the resected specimens positive smears were obtained in 47 cases (84%), a higher rate being obtained from filled-in cavities than from open cavities. Positive cultures or guinea-pig inoculations were obtained only in 16 cases, a rate of 28.5%.

The viability of the tubercle bacilli in the resected specimen was correlated with preoperative sputum and cavity status (Table X). It was found that 41% of patients with positive sputum and 20% of those with negative harboured viable organisms in the lesions. Furthermore, 33 open cavities contributed viable organisms in 10 cases (30%) and 23 closed cavities in 6 cases (26%).

TABLE X.

CAVITARY LESIONS
VIABILITY OF M. TUBERCULOSIS IN RESECTED SPECIMENS
SPUTUM AND CAVITY STATE CORRELATION
(6-12 Months Chemotherapy)

Sputum status	*Viable organisms in resected lesion*		*%*	*Cavity status*	*Viable organisms in resected lesion*		*%*
Positive	22	9	40.9	Open	33	10	30
Negative	34	7	20.5	Closed	23	6	26

The combination of negative sputum and closed cavity does not permit prediction of viability of the organisms in the resected lesions; in fact 19 such cases produced viable organisms in 5 instances (26%).

Pathological changes.—The analysis of the reports on gross and microscopic examination of the operative specimens has revealed the following: One group of cavities did not close under prolonged chemotherapy and the cavity wall remained characteristically infiltrated by typical tuberculous granulation tissue containing stainable tubercle bacilli.

A second group closed, resulting either in a sclerotic scar or a residual fibrocaseous lesion. Histological sections proved the cavitary origin of the lesion, but the fibrotic component overshadowed the caseous infiltration which was replaced by ordinary granulation tissue.

The third group were the so-called filled-in cavities which radiologically might easily have been mistaken for tuberculomatous lesions had there not been proof of previous cavitation. The content of these inspissated cavities varied according to the duration of closure, the oldest containing chalky material, at times sterile or more often with a low bacillary content.

The fourth group were the so-called bullous cavities, thin-walled, fibrotic, smooth and glistening, much resembling an emphysematous bulla or an air cyst. The draining bronchus was often patent and the broncho-cavitary junction epithelialized.[9, 10] At times a little residual necrotic material was discovered in such a cavity, but more frequently it was clean or no tubercle bacilli could be demonstrated. This peculiar type of bullous cavity became more common after prolonged chemotherapy, particularly when isoniazid was used in combination with streptomycin, as reported by others.[11]

DESTROYED LOBES OR LUNGS

This group consists of cases with massive fibrocaseous cavitary processes complicated by bronchiectasis, bronchial stenosis, collapse, bronchopleural fistula or empyema. There were 48 such lesions; all but 7 were from far advanced cases with a 5-15 years' history of tuberculosis.

Preoperative chemotherapy.—This ranged from six to 24 months. Most of the patients in this group had had previously short, irregular courses of treatment and half of them had developed streptomycin resistance. However, resistance could not be assessed in many because cultures did not grow in spite of the positive sputum concentrates. Radiological and clinical improvement was steady up to the 18th month, becoming slow and minimal thereafter. All resistant cases improved although the sputum did not convert.

Sputum bacteriology.—On admission sputum in all cases but one was positive. After 6 to 24

TABLE XI.

DESTROYED LOBES OR LUNGS
SPUTUM BACTERIOLOGY AFTER
6-24 MONTHS OF CHEMOTHERAPY

Sputum	*Admission*	*Preoperatively*
Positive	47	24
Negative	1	24
Total cases	48	Conversion rate 50%

months of chemotherapy, 24 cases (50%) remained positive (Table XI).

The sputum conversion was usually obtained at about the 8th to 12th month of treatment; no case converted after the 18th month of chemotherapy, although serial radiological examination showed well retrogressed and stabilized lesions.

Bacteriology in resected specimens. — There were 25 lobectomies and 23 pneumonectomies, mostly pleuropneumonectomies. There were a single surgical death (due to pulmonary embolism), three minor complications and two late tuberculous complications. The latter appeared in two patients, sputum positive and drug resistant, between the 3rd and the 5th month postoperatively. It is interesting that all sputa became negative after surgery. Many other drug-resistant patients went through operation with no complications whatsoever, substantiating our principle that drug resistance is not a definite contraindication to surgery, although one must be prepared to accept a little higher complication rate. When we review this group of patients who represent the bulk of our far advanced and poor risk cases, some absolutely desperate, with repeated sanatorium admissions and long segregation from the community, we cannot but feel that surgery has achieved something for these patients. The only late fatal outcome we have had in two hundred resections is the case of tuberculous meningitis developing three months after operation on a drug-resistant patient. It is interesting that his sputum became and remained negative after operation, although he developed the fatal meningitis. Most of the patients are now discharged and well.

TABLE XII.

DESTROYED LOBES OR LUNGS
BACTERIOLOGY ON RESECTED SPECIMEN
(6-24 MONTHS OF CHEMOTHERAPY)

No. cases	*Positive smear*		*Positive Cult./G.P.*	
48	35	73%	13	27.1%

The resected specimens yielded positive smears in 73% of the cases and positive cultures or guinea-pig inoculations in 27.1% (Table XII). When resistant organisms were discovered in the sputum they were also viable and resistant in the resected lesion.

DISCUSSION

A basic principle meticulously observed in our series of resections was to operate at a time when maximum effect of chemotherapy had been obtained and substantiated by serial radiographs. Some of the patients reached the "target point" as defined by D'Esopo, others failed. However, both groups clinically and radiographically had achieved a peak benefit from chemotherapy beyond which further improvement was minimal or nil. At this stage of treatment sputum was often negative even on cultures, but radiographs would show in the majority of cases obvious pathological changes as expressed by wide open cavities, dense lesions, marked bronchiectasis, or destroyed lobes or lungs. By this time all patients had gained weight and strength, the symptoms had subsided, the blood picture and erythrocyte sedimentation rate were normal and they appeared "as good as they could be" when the attending physicians presented them before the medico-surgical conference. This stage of treatment, where decision had to be made as to surgical intervention, was identified as the *"therapeutic critical point."* It was so defined:

1. Maximum radiological improvement and stabilization of the lesions.
2. Bacteriological findings on the sputum non-conclusive—at times negative on both concentrate and cultures, often paradoxical, namely positive on smear, negative on culture.
3. Erythrocyte sedimentation rate and blood picture within normal limits.
4. Satisfactory clinical picture characterized by absence of constitutional symptoms and physical findings related to gross destruction of areas of parenchyma, or in many cases entirely negative.

It was observed that the "therapeutic critical point" was reached between the 6th and the 18th month of chemotherapy in the great majority of cases. In none of the far advanced cases with positive sputum at the end of 18 months of drug

treatment was the sputum converted when chemotherapy was prolonged to 24 months. After operation chemotherapy was administered as a rule for 6 months, exceptionally for 8-12 months.

With this background in mind, the review of the bacteriological data summarized in Table XIII stimulates some interesting considerations.

TABLE XIII.

SUMMARY OF BACTERIOLOGICAL DATA IN 132 RESECTIONS
(PREOPERATIVE CHEMOTHERAPY 6-24 MONTHS)

TUBERCULOMATOUS (*14 cases*) (*6-8 months' chemotherapy*)	FIBROCASEOUS (*14 cases*) (*6-12 months' chem.*)	CAVITARY (*56 cases*) (*6-12 months' chem.*)	DESTROYED (*48 cases*) (*6-24 months' chem.*)
SPUTUM BACTERIOLOGY			
Sputum conversion 88.8%	Sputum conversion 100%	Sputum conversion 55.4%	Sputum conversion 50%
		Cavity closure 41.7%	
RESECTED SPECIMEN BACTERIOLOGY			
Smear 93% / Cult./G.P. 28.5%	Smear 100% / Cult./G.P. 21.4%	Smear 84% / Cult./G.P. 28.5%	Smear 73% / Cult./G.P. 27.1%

Of 132 resected specimens, 82.5% positive on smear, 27.2% viable on culture/G.P.

Tuberculomatous and fibrocaseous lesions had an average sputum conversion rate of 94%, whereas cavitary lesions and destroyed lobes and lungs had an average rate of 53%. The discrepancy is explained if one considers the differences in pathological lesions and the not uncommon drug resistance which develops in the more severe and chronic types of disease. Obviously these figures cannot be generalized for they refer to a selected group of patients requiring surgery.

In the resected specimens tubercle bacilli were demonstrated by smear in 82.5%. However, positive cultures or guinea-pig inoculations were obtained in 27.2%. Persistence of open cavity and positive sputum were useful but not definite criteria to predict the recovery of viable organisms from the resected specimen unless associated with preoperative drug resistance. Viable organisms were obtained from 28.5% of the tuberculomatous, from 21.4% of the fibrocaseous, from 28.5% of the cavitary lesions and from 27.1% of the destroyed lobes or lungs. The distribution of these findings revealed no significant difference between cavitary and non-cavitary, or between minimal and far advanced lesions. This is somewhat at variance with findings of other workers[1, 3, 5, 7, 8] who generally obtained a much higher viability rate in the open cavity group than in those with closed lesions.

To bring these observations into one coherent picture, the following framework of hypotheses has been devised. In every case there is a peak therapeutic effect of drugs beyond which further improvement is practically nil. The lesions resected at this stage of treatment, indicated as the "therapeutic critical point," showed tubercle bacilli by microscopy in over 80% of the operative specimens, and in 27% the bacilli were culturable or pathogenic in guinea pigs. The percentage distribution of the organisms, both stainable and viable, was practically the same regardless of the type of lesion and extent of disease, provided there were areas of caseation. This suggests that at this stage of treatment whatever focus of infection remains is confined to areas of caseous necrosis. It is well known[13] that present anti-tuberculous agents are effective in early lesions when the organisms multiply actively. The drugs diffuse into the caseous matter[13] but have little or no effect on the bacilli when they have stopped multiplication and assumed a "resting state." Whether this "dormant state" may be due to the effect of drugs, to the effect of antagonistic substances produced by caseous necrosis or to differing host-parasite relations is a matter of speculation. A re-evaluation of current bacteriological techniques has been undertaken by many investigators[14-17] and evidence is accumulating that present methods are inadequate in this era of chemotherapy of tuberculosis. It is also known[13] that advanced caseous necrosis by destroying the cellular framework of the diseased tissue does not offer any support for the reparative processes, and it is suspected that at this stage of disease chemo-

therapy has no healing effect. Since the presence of necrotic areas was the common denominator in the four types of lesions, our findings seem to corroborate the hypothesis that caseous necrosis is pathologically and possibly bacteriologically the same entity whether the process is minimal or far advanced and whether the lesion is a tuberculoma, a cavity or a caseous pneumonia.

SUMMARY AND CONCLUSIONS

One hundred and sixty-two consecutive pulmonary resections for tuberculosis are analysed; the criteria of acceptance and classification are given. The net series consists of 132 cases; tuberculomatous 14, fibrocaseous 14, cavitary 56, destroyed lobes or lungs 48. Preoperatively all cases were treated by drugs in different combinations to the stage of maximum clinical and radiological improvement. This stage of treatment, called the "therapeutic critical point", was usually reached between the 6th and 18th month of drugs. The sputum conversion rate was 94% in cases with tuberculomatous and fibroproductive lesions, 53% in cases with cavitary lesions and destroyed lobes or lungs. The cavity closure rate was 41.7%.

Tubercle bacilli were demonstrated by smear in 82.5% of the resected specimens, but positive cultures and/or guinea-pig inoculations were obtained in only 27.2%. The percentage distribution of viable organisms was the same regardless of the type of lesion or extent of disease. These findings have suggested the hypothesis that at the "critical point" whatever focus of infection remains is confined to areas of caseous necrosis which pathologically is the same entity and bacteriologically offers the same chances of harbouring viable organisms whether the lesion is a tuberculoma or a cavity or a caseous pneumonia.

Practical implications of this are:

1. So-called sterilization of tuberculous lesions by present therapeutic agents is possible in the early stages of disease before advanced caseation develops.
2. In advanced lesions, beyond a certain "critical point" of treatment, drug therapy produces little apparent change.
3. When necrotic areas remain after the "therapeutic critical point" has been reached, the chances are that a great number of tubercle bacilli are demonstrable by microscopy, and at least in one-quarter of the cases they are viable by current methods of culture or guinea-pig inoculation.
4. There is no definite criterion for predicting before operation which lesion will contain viable organisms.
5. Therefore, in our opinion, surgical excision is the treatment of choice of residual necrotic areas provided that the risk is slight, as it was in this series of 162 consecutive resections with a surgical mortality of only 0.6% and minor complication rate of only 7.4%.[18]

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RÉSUMÉ

L'étude pathologique et bactériologique des lésions réséquées doit etre encouragée aux fins de définir le but et l'application de la réséction dans la tuberculose pulmonaire.

Cent soixante deux (162) réséctions consécutives furent analysées.

Critères de sélections: (1) Histoire clinique du cas. (2) Examen complet bactériologique et pathologique du spécimen opératoire. (3) Etiologie tuberculeuse du procés.

Trente cas furent repoussés, ne répondant pas aux susdit critères. La série nette consiste de cent trente deux (132) cas classifiés en tuberculomes, lésions fibro caséeuses, lésions caverneuses, et destruction totale des lobes ou poumons. Aprés 6-12 mois de chimiothérapie, les tuberculomes et les lésions fibro caséeuses avaient une moyenne conversion du crachat de 94%, lorsque celle des lésions caverneuses etait du 55.4 pour cent. La cicatrisation des cavités était seulement du 41.7 pour cent. Aprés 6-24 mois de chimiotherapie, les lobes ou poumons détruits avaient une conversion du crachat du 50 pour cent.

Dans les spécimens opératoires les bacilles tuberculeux etaient démontrés par microscopie en 82.5%; mais seul le 27.2% etait positif dans les cultures ou par inoculation au cobaye. Des organismes viables furent trouvés:

Dans le 28.5% des tuberculomes.
Dans le 21.4% des lésions fibro caséeuses.
Dans le 28.5% des lésions caverneuses et
Dans le 27.1% des lobes ou poumons détruits.

Pour expliquer ces résultats, on présente la nouvelle conception du dit "point critique" thérapeutique.

Ceci est représenté par le stage de maladie ou la chimiothérapie a atteint le maximum d'amélioration clinicale et radiologique, ce qui ne signifie pas nécessairement la conversion du crachat ou la cicatrisation des cavernes. Ce maximum est obtenu entre le sixième et le dix-huitième mois de chimiothérapie, selon le type et l'étendue du procès.

A ce point les bacilles tuberculeux sont démontrés par microscopie dans le 80% des specimens opératoires, mais seulement dans un quart sont ils cultivables et transmissibles au cobaye. Le pourcentage d'organismes viables est le même pour les quatre types de lésions, présumablement parce que à ce "point critique" le restant de l'infection est confiné dans les zones de nécrose caséeuse qui au point de vue pathologique est la même entité, même si la lésion soit un tuberculome ou une cavité ou bien une pneumonie caséeuse.

Nous ne savons pas si cette situation est dû à l'effet des antibiotiques sur les bacilles tuberculeux ou à la mutation spontanée de ceux-ci ou bien aux différentes relations "hôte-parasite."

Les conclusions pratiques des susdit faits sont:

1. La résolution et la dite stérilisation des lésions tuberculeuses par les agents anti-tuberculeux sont possible dans la phase précoce de la maladie.
2. Au delà du "point critique" la chimiothérapie produit de changements minimes.
3. Lorsque la nécrose caséeuse s'est manifestée, un certain nombre de lésions conservera des organismes viables même aprés avoir rejoint le "thérapeutique point critique."
4. Il n'y a aucun critère pour prévoir avant l'opération l'état bactériologique des lésions nécrotiques visibles dans les radiographies.
5. Pour cette raison, même aprés la chimiothérapie prolongée l'excision chirurgicale des lésions nécrotiques semble être le traitement de choix, pourvu que le risque soit moindre. Les résultats obtenus dans la série des cent soixante deux (162) réséctions consécutives, avec la mortalité de 0.6% et taux de complications au dessous de 7.4%, semblent appuyer le susdit point de vue.

HYALINE CARTILAGE: DEGENERATION AND REGENERATION*

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THE APPEARANCE of hyaline cartilage is familiar to us all, as is its smooth resilient feel. It is developed from the mesenchyme. It forms a remarkable elastic covering for the ends of bones forming a joint. Though devoid of blood supply and nerve supply, it maintains functional efficiency in dealing with strains of very great magnitude. There is much as yet incomplete in our knowledge of its structure and life history. We owe much and will owe more to the work of the biochemist and the histologist, and to animal experiment. It is gratifying to us as practitioners to know that the orthopædic surgeon has been able to contribute his mite from the records of clinical experience.

There are three histologically recognizable elements in the make-up of hyaline cartilage, cells, ground substance, and fibrils. The cells are modified mesenchymal cells and are known as chondrocytes. The ground substance is amorphous; it is a mucopolysaccharide, containing sulphuric acid; it is believed to be chondroitin sulphate. When this ground substance is dissolved out, the third element, the fibrils, are left behind. These fibrils are collagenous in character. They can be changed into gelatine, but the process is not reversible.

THE CELLS

Near the free surface the cells are small and flattened. These are the youngest cells. More

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deeply they are situated in definite lacunæ, which may contain one or more; sometimes the cells are grouped in pairs or fours. In such a case the formation is referred to as a cell nest. At a still deeper level the cartilage cells tend to be arranged in columns; deep to this layer there is a zone of calcified cartilage, containing no cells. This calcified layer abuts on the subchondral bone.

THE GROUND SUBSTANCE

The ground substance, cement, or matrix has been the subject of considerable study during the last few years; in spite of this, there is much to be learned regarding its chemical constitution and reactions. It is known to be a solid gel, a sulphated mucopolysaccharide. It is definitely acid in reaction and is extremely susceptible to the action of weak alkali. It is believed to be secreted by the cartilage cells. It is this cement substance that confers on hyaline cartilage a "perfect elasticity, given time, to intermittent pressures." This elasticity, it is held, is associated with exudation and reabsorption of water, a theory supported by the observation that articular cartilage increases in thickness during exercise. The water which is bound in the solid gel serves as the "dispersion medium" for nutritive material, organic or inorganic. It has been repeatedly shown that pressure and movement are essential for the continued well-being of articular cartilage. A clinical application of this fact is that there is a time limit beyond which reposition of a dislocated joint, e.g. a shoulder, though anatomically feasible is physiologically unrewarding.

THE COLLAGENOUS FIBRILS

The collagenous fibrils serve to bind and give strength to the more friable matrix. Originating in the calcified layer, they pass vertically towards the surface; as they approach the latter they curve so that they gradually run parallel to the surface, forming a dense feltwork in the interstices of which there is little or no ground substance, and chondrocytes are few. They then curve downwards again, becoming perpendicular to the surface, and come to an end in or about the calcified layer. In this way they form a series of arcades. Near the periphery of the articular surface these fibres blend with the periosteum over the bone and with the fibrous substratum of the synovial membrane. It follows from this arrangement that the exposed surface of hyaline cartilage is composed almost entirely of collagenous fibrils. These are relatively tough, and more resistant to insult by trauma or chemical action than is the relatively susceptible ground substance. Between the bundles of fibrils there have been described structures like little spiral springs, presumably collagenous in nature, called "chondrothones." I have not been able to find out much about them.

Matthews investigated the ratio of collagen to ground substance in human articular cartilage. He found the ratio higher in the shoulder than in the knee and concluded that the stress of weight-bearing demanded a larger proportion of cement substance. In osteoarthritic joints the ratio was still higher, indicating a proportionately greater loss of ground substance.

THE NUTRITION OF CARTILAGE

There are three possibilities to be considered as a source of nourishment for the chondrocytes: blood vessels of the subchondral bone, capsular or perichondrial blood vessels, and synovial fluid. It is generally accepted that the greater part of the nutriment is derived from the synovial fluid. Strangeways propounded this view in 1920, and laid the blame for degenerative changes in the joint on alterations in the nutritive value of the fluid. This latter deduction is not now acceptable.

In the condition of osteochondritis dissecans, there is a small nodule of bone separated from the parent part of the epiphysis. This nodule remains covered by articular cartilage, if it does not separate as a loose body. Sometimes this cartilage appears to be normal; often it is yellowish in colour. Microscopical examination shows that the nodule of bone is dead and the overlying cartilage shows varying degrees of nutritional disturbance. Some of the cells are dead and others appear to be normal. If, as sometimes happens, the necrotic nodule becomes revascularized, the cartilage cells may improve in vitality and staining properties. This seems to indicate that although the major part of nutrition of cartilage is derived from synovial fluid, an appreciable amount must come from the subchondral bone. How this nutritive material makes its way through the calcified layer is not quite clear, but presumably it is able to do so.

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No conclusive evidence has been forthcoming as to the mechanism of nutritive exchange. By some it is assumed that it takes place along the system of fibrils. Others look upon it as a purely physical process, the result of alternate pressure and suction. If this be so, it furnishes an explanation of the necessity for active use of a joint to maintain the health of articular cartilage.

Studies have been made of the metabolism of cartilage. It is found that respiration is almost nil. Its metabolic rate is about one-tenth that of connective tissue. This suggests that, once growth is over, the capacity of hyaline cartilage for repair would be very small, a conclusion borne out by experience. A problem that has not been cleared up is that of "wear and maintenance" growth of cartilage. It would seem that in normal circumstances lubrication of a joint is sufficient to ensure minimal erosion; such repair as is called for is provided by amitotic division of cartilage cells.

THE CALCIFICATION OF CARTILAGE

If we accept the views of Robison in regard to the action of phosphatase, it is not very difficult to accept the reasoning which explains the appearance and later disappearance of calcified cartilage in the neighbourhood of the growing disc at the end of a long bone. Why, however, does ossification not proceed right to the surface of the end of the bone? Why is a cap of hyaline cartilage left, and what is the meaning of the calcified layer that separates the hyaline cap from the subchondral bone? There are no cells in this calcified layer; nutritive substances could diffuse only with difficulty if at all through calcified cement substance, and yet we are assured that the presence of living cells seems to be necessary for the permanence of calcified intercellular substance. The chondrocytes adjoining the calcified layer are the largest and oldest members of the cell population, and it is assumed that they are responsible for secreting alkaline phosphatase; otherwise there would be no calcified layer. From another point of view it would seem that the calcified layer functions as a protective or insulating layer holding back the highly vascular and (if one may use the expression) aggressive subchondral bone from invading the hyaline territory. When, as the result of trauma, the calcified layer is broken there is prompt incursion of subchondral bone through the gap. Towards the periphery of the articular surface the calcified layer is very thin and is likely to fracture under the tension strains associated with the capsule of the joint. It seems reasonable to consider this process as a factor in the development of marginal osteophytes. It furnishes at least a working hypothesis to account for the presence of osteophytes along the vertebral column or around the upper rim of the acetabulum.

SYNOVIAL FLUID

Inasmuch as the vitality of hyaline cartilage is so closely bound up with synovial fluid, it is of interest to examine some of the properties of this substance. It is important to think of a joint as essentially a tissue space; synovial tissue is not a membrane, and the cells of synovial membrane are not an endothelium but are slightly modified connective tissue cells. The synovial fluid is not a secretion from these cells; it is, in essence, tissue fluid. It is "a dialysate in equilibrium with blood plasma." The main point of difference from ordinary tissue fluid is the presence of mucin. Like the ground substance of hyaline cartilage, mucin is a polysaccharide complex. In the case of hyaline cartilage the polysaccharide is sulphated; in the case of mucin, it is not sulphated. This mucopolysaccharide is probably formed by the connective tissue cells surrounding the joint. Synovial fluid is very viscous, contains relatively few cells, and, as it contains no fibrinogen, does not clot. The mucin is believed to serve three functions: (1) It lubricates. (2) In virtue of its high base-binding power, it aids in the regulation of calcium equilibrium. (3) It affects the transfer of water between plasma and synovial fluid.

Synovial membrane has much greater permeability than a true membrane, and this permeability is much increased in inflamed joints. Normally the proportion of albumin to globulin in synovial fluid is about 20 to 1. Little is known about the enzymes of normal synovial fluid. Amylase, protease, and lipase are present; there is no catalase. The activity of alkaline phosphatase in normal synovial fluid is much lower than in blood serum. The highest concentration of mucin is found in osteochondromatosis. The reason for this is not known. In traumatic and degenerative joint changes there is no change in unit concentration of mucin. The administration of ACTH or cortisone to rheumatoid arthritic patients in whom the viscosity was diminished resulted in dramatic improvement. Meyer has

recently identified the mucin of synovial fluid with hyaluronic acid. This is believed to be a normal component of synovial membrane; it is washed into the joint by tissue fluid passing from the capillaries of synovial membrane into the joint cavity.

HYDROGEN ION CONCENTRATION

There are few exact reports. Synovial fluid is said to be weakly alkaline to litmus. The average pH found post mortem was 7.40.

LUBRICATION

The mechanism is that of the fluid film. There is some solid friction when the speed or the eccentricity of movement is insufficient to maintain a pressure film. The fluid film is said to be able to withstand a pressure of 900 lb. per square inch, a load that will crush bone.

AGE CHANGES

As age progresses, the collagenous fibril component of hyaline cartilage becomes increasingly predominant. "The hyaline cartilage of youth may become the fibrous cartilage of senility." It has been said that the transformation of hyaline into fibrous cartilage is one of the earliest signs of aging in the body.

DEGENERATION

The two main factors are probably age and trauma. The changes due to age have been studied extensively and intensively by Bennett, Waine and Bauer in a series of knee joints covering 10 decades. Changes were first observed in the second and third decades. The cartilage lost its bluish-white colour and became more yellowish and opaque. While firmer, there was some loss of elasticity. At the same time the surface layers showed small blisters or linear grooves or pits in the areas where weight-bearing is concentrated. Microscopically there were slight surface irregularities, small elevations and shallow depressions from which shreds of fibrillar tissue had been detached. There was abnormal staining of the matrix. The matrix itself appeared macerated, and the fibrillar pattern was accentuated. Succeeding years enhanced all these features. The surface became velvety and spongy as a result of loss of the ground substance and exposure of the collagen fibrils. The clefts and fissures passed right down to the subchondral bone, and fragmentation of the calcified layer was much increased. This was not invariably so. In many human joints, even with considerable cartilage change, the calcified layer and the subchondral bone remained intact. For the most part, however, as degeneration progressed, the calcified layer showed multiple fractures and gaps of increasing size. Sometimes there were dissecting fissures between the non-calcified and the calcified parts of the cartilage.

It has been generally assumed that trauma plays a major part in the degenerative process. Where the fibrils of articular cartilage change direction to blend with the substratum of synovial membrane and ligament, the stresses are mainly tension stresses. It is tension stresses that we associate with the development of osteophytes elsewhere in the body, as in the spurs so commonly found about the olecranon or the calcaneus. A recent paper claims that the osteophyte is "a biological response in a tissue sick from underwork." This is a picturesque and challenging dictum.

There are several other factors which deserve consideration. One of these is *circulatory insufficiency*—poor blood supply. This theory is associated with the name of Axhausen. It was disputed by Pommer and discussed by Kling who concluded on the basis of three cases of thromboangitis obliterans and ten of arteriosclerosis that the influence of the circulation was negligible. Sympathectomy has also been employed as an experimental measure. No constant changes have been observed in the joints. *Constitutional and heredo-familial factors* have been repeatedly emphasized. Silberberg and Silberberg speak of the degeneration as "probably genetically determined." These investigators lay stress on the need for hormonal balance. In animals, anterior hypophysis transplants or Antuitrin G (growth hormone) promotes growth changes, and in human subjects cartilage responds in a similar way. Removal of sex glands results in early proliferative processes similar to those produced by anterior hypophysis hormones. The combination is very effective in producing severe articular lesions. Conversely, administration of thyroid and œstrogenic and androgenic hormones leads to a condensation of cartilage. Hypothyroidism is said to aggravate joint lesions as after the menopause. The conclusion is that the growth hormone elicits a maximum growth response in cartilage by increasing water content and nitrogen retention. The growth capacity is prematurely exhausted,

and degenerative changes appear. In contrast to this is the action of thyroid and œstrogenic and androgenic substances. It is probably necessary to have endocrine equilibrium to maintain a physiological state.

REGENERATION

A fairly large mass of experimental evidence proves that a certain amount of repair is possible after injury. The repair process occurs more readily near the perichondrial margin and on the weight-bearing surfaces. There are three possible sources of repair: (1) proliferation of chondrocytes; (2) proliferation of vascular connective tissue from the perichondrial margins; (3) ingrowth of vascular connective tissue from the subchondral bone. According to Bennett and Bauer, all three processes may play a part. A crevice in the cartilage seems to afford the most favourable surroundings for repair from existing cartilage cells.

Carey and Zeit found regeneration of cartilage to take the place of an excised patella provided "adequate mechanical conditions" were present, i.e., "a normally mobile exercising articulation with the soft parts replaced."

Shands carried out a study of hyaline cartilage regeneration with special reference to the depth of the defect created. He found that no evidence was visible in less than four weeks, but it was clear after twelve weeks. He placed the order of appearance as follows: (1) fibrin; (2) granulation tissue; (3) connective tissue; (4) cartilage cells in connective tissue; (5) fibro-cartilage; (6) hyaline cartilage. The most complete regeneration was found where subchondral bone was involved.

CLINICAL CASES

1. Mrs. A.G. was admitted to Winnipeg General Hospital with a history of pain and stiffness in the right hip. This dated back to a fall some 10 years previously. On March 4, 1941, arthroplasty of the right hip was performed. The operation was undertaken with some reluctance in view of the fact that one breast had been removed for carcinoma in April 1940, but relief from pain seemed worth while. She was readmitted to hospital on February 2, 1942, and died on March 12. The autopsy report was as follows: "Secondary metastases in pleura, in liver, in vertebræ. Right hip, there are numerous exostoses above the acetabulum. Capsule is continuous and of normal thickness. On incision, vitallium cup in place; it moves both in acetabulum and on head of femur. Microscopically, the head of the femur is covered with collagenous fibrous tissue. No cartilage cells are seen. Underlying bone irregularly rarefied. There is one small deposit of carcinoma cells in the cancellous bone."

2. D.S. aged 58, a band leader, underwent vitallium cup arthroplasty in 1946 for osteoarthritis. The result was unusually good. He died in December 1949, from bronchogenic carcinoma with supraclavicular metastases, three years and eight months after operation. At autopsy, the joint capsule of the hip was complete and normal in thickness. The vitallium cup moved freely in the acetabulum and the femoral head moved freely in the cup. The head of the femur was covered by a smooth bluish surface resembling articular cartilage. Microscopically, the head of the femur under the vitallium cup showed cancellous bone with marrow spaces. The bone terminated in a fairly regular line of ossification merging into cartilage consisting of an eosinophilic matrix with groups of definite cartilage cells. This merged imperceptibly into an articular surface layer where the cells were elongated and parallel to the articular surface. There had been replacement of hyaline cartilage after trimming of the head of the femur at operation.

3. J.P. was aged 71 at the time of admission to Winnipeg General Hospital in June 1943. He had bilateral osteoarthritis of the hip-joint of many years' duration. In his active years he had had much to do with horses. He was barely able to get about and pain was constant and severe. On June 16, 1943, a vitallium cup arthroplasty was performed on the left hip. The result was, to him, quite satisfactory and he urged that the other hip also be treated. On January 5, 1945, the right hip also underwent vitallium cup arthroplasty. In spite of his age (73) he improved and was discharged from hospital on February 9. Thereafter he was able to get about reasonably well. On September 21, 1953, he was again admitted to hospital with severe abdominal pain and dysuria. He was now 81 years old. On September 29, he died and at autopsy both hip-joints were removed. The pertinent portion of the autopsy report (Dr. D. W. Penner) is as follows.

"Pelvis and femurs. Both hips are the site of previous operative procedure. The muscles of the pelvis and thighs are fairly well developed and preserved for a man of this age. On going through the site of previous operation, remarkably little tissue reaction remains. There is some scarring and thickening of the joint capsule with a few external adhesions but this is rather less than might be expected. Lower limbs show good movement in all directions but the exact range of movement cannot be determined due to rigor mortis. On opening into the hip joints both sides are seen to be similar. There are bilateral cups present. Articular surfaces of both heads of femur and acetabulum are smooth, and covered by thin, mucinous, normal-appearing joint fluid. There is a slight amount of lipping about the periphery of both the head and the acetabulum. This is very minor. Cross-section of the head and acetabulum shows the articular surfaces to be covered for the most part by a fairly uniform articular cartilage which measures from 0.5 mm. to 2 mm. in thickness. In some areas no articular cartilage is grossly present but the surface is smooth and at these sites is presumably covered by a thin layer of fibrous connective tissue.

"Microscopically, the picture is essentially the same in all areas. Articular surfaces are covered for the most part by normal-appearing hyaline cartilage. In a few areas the superficial portion of the cartilage is replaced by fibro-cartilage, but only in a few areas is there absence of cartilage cells with only connective tissue present. The underlying bone appears essentially normal. Marrow is for the most part fat-replaced. In a few areas it is replaced by fibrous tissue."

COMMENT

These three cases represent very different individuals. The first was an obese elderly woman in poor health. Her general activity was of rather low grade. The specimen was examined one year after operation. The second

patient was much younger; he obtained a remarkably good result and until a short time before his death led a very active life. The specimen in this case was obtained more than three years after operation. The third patient was definitely senile; the range of movement at the hip-joints was not extensive in any direction, and his activity was decidedly moderate in character and amount. The specimen in this case was obtained 10 years after operation. In spite of restricted use, both hip-joints show considerable re-formation of cartilage.

If conclusions can be drawn from such a small series of cases it would appear that fibro-cartilage can be formed under a vitallium cup within a year, and that hyaline cartilage, plainly detectable after three years of activity, can be reformed even at an advanced age and with limited functional use. There is no possibility that remnants of the original hyaline cartilage were the immediate precursors of the new-formed cartilage covering. The cartilage would seem to have developed from fibroblasts under the combined stimulus of pressure, weight-bearing, and friction. It is interesting that synovial fluid apparently normal in character should have been present within the joint. An opportunity to study it was missed. Should another occasion present itself, more careful examination of the fluid will be carried out.

My thanks are due to Dr. D. W. Penner for the autopsy report on Case 3.

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RÉSUMÉ

L'auteur rappelle la structure histologique et la biochimie du tissu cartilagineux. La nutrition des chondrocytes peut s'effectuer par les vaisseaux des régions osseuses sous-chondrales, les vaisseaux capsulaires ou périchondriaux et surtout par le liquide synovial. Il se pourrait que l'échange entre le cartilage et le liquide synovial se produise au cours des variations de pression de ce dernier, ce qui expliquerait l'importance de l'activité d'une articulation dans l'entretien de bons cartilages. L'usure cartilagineuse d'une articulation normale est minime et la division amitotique des cellules semble suffisante pour combler les déficits. Selon Robinson, la raison pour laquelle l'ossification des os longs s'arrête à la couche de cartilage calcifié serait dans la présence des gros chondrocytes de la région avoisinante qui sécréteraient la phosphatase alcaline. Si cette couche calcifiée, agissant à la manière d'une barrière vis-à-vis de l'invasion vasculaire osseuse, vient à manquer à cause d'un traumatisme quelconque, l'os infiltre immédiatement le cartilage. L'auteur offre cette hypothèse comme pathogénèse des ostéophytes. La mucine du liquide synovial semble remplir trois fonctions: lubrification, régulation de l'équilibre du calcium, et facilitation de l'échange de l'eau avec le plasma. La grande perméabilité de la membrane synoviale normale est encore accrue dans les états imflammatoires. La mince couche lubrifiante de liquide synovial est censée pouvoir résister à une pression de 900 lbs. par pouce carré. Avec l'âge, le cartilage hyaline se transforme lentement en cartilage fibreux; de blanc bleuâtre, il devient jaunâtre, opaque, plus ferme, et perd de son élasticité. Les traumatismes jouent un rôle prépondérant dans ce processus de dégénérescence. L'hormone de croissance stimule le tissue cartilagineux en augmentant son contenu aqueux et la rétention azotée. La capacité de croissance s'épuise vite et la dégénérescence suit.

D'après Shands, les stages de la régénération du tissu cartilagineux se produisent dans l'ordre suivant: déposition de fibrine, formation de tissu de granulation, tissu conjonctif, apparition de cellules cartilagineuses dans le tissu conjonctif, formation de fibro-cartilage produisant enfin le cartilage hyalin. Il semble que le fibro-cartilage puisse se former sous une coupe de vitallium en moins d'un an et que le cartilage hyalin puisse suivre dans trois ans d'usage d'une telle articulation, même chez les vieillards.

L'auteur présente 3 cas cliniques à l'appui de ses dires. M.R.D.

In the Victorian age the doctor was satisfied to save life and ease pain. With the growth of medical knowledge he has essayed to cure disease, and with some success. Now he is required to do all that and more. He is now to remove his patient's disability and restore him to his place as a happy earning member of the community. Disability rather than disease will interest the doctor of the future—or rather he will be interested in disease only as a cause of disability, interpreting disability not only as connoting impairment of earning capacity, but also as a threat to life, or interference with the comfort and enjoyment of life.—H. Hastings Willis, *M. J. Australia*, 1: 899, 1955.

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LOW BACK PAIN. THE HYPEREXTENSION SYNDROME*

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LOW BACK PAIN can be subdivided into three main groups: (1) viscerogenic backache, (2) psychogenic backache, (3) spondylogenic backache.

Spondylogenic backache, that is to say back pain derived from disorders of the spinal column and its associated structures, may again be subdivided into two main groups. The first group consists of those cases in which the pathological basis for the patient's symptoms is readily apparent (Table I). This group presents little difficulty in diagnosis, and treatment is along well-established lines. Unfortunately, probably less than 5% of patients seen in office practice fall into this category. In the remaining 95%, the pathological basis for the patient's symptoms is extremely difficult to assess (Table II). Probably the commonest causal factor of this type of back pain is disc degeneration and its sequelæ.

TABLE I.

ETIOLOGY OF SPONDYLOGENIC BACK PAIN.

GROUP I. (Pathological basis of pain obvious).	
(A) Sequel of fractures and fracture dislocations:	(Interference with mechanics of, or damage sustained by, the posterior joints.)
(B) Neoplasms:	Benign Malignant—primary secondary
(C) Infections:	Acute pyogenic Chronic pyogenic Granulomatous
(D) Structural defects:	Spondylolysis Spondylolisthesis Pseudospondylolisthesis Scoliosis
(E) Miscellaneous:	Herniated disc Paget's disease Osteoporosis (? pain due to trabecular fractures) Calvé's disease Ankylosing spondylitis

Unfortunately the terms "disc degeneration" and "disc" are now being so loosely used as to lose much of their significance. Particularly is there confusion between the term "herniated disc" (and its synonyms "prolapsed disc," "protruded disc," "ruptured disc") and disc degeneration. The term "disc degeneration" denotes structural and functional changes occurring in an intervertebral disc, initiated by increasing age, conditioned by constitutional and nutritional factors, and aggravated by trauma. Disc degeneration may or may not go on to produce side-effects capable of giving rise to symptoms. The term "herniated disc" denotes an accident—usually occurring in the course of disc degeneration—as a result of which there is extrusion of components of the disc, which may be of sufficient size to cause nerve root compression or irritation.

TABLE II.

ETIOLOGY OF SPONDYLOGENIC BACK PAIN.

GROUP II. (Pathological basis of pain obscure).	
(1) Soft tissue lesions	
(2) Disc degeneration and its effects:	(*a*) Postural deformities. (*b*) Unstable segment. (*c*) Posterior joint subluxation. (*d*) Posterior joint arthritis.
(3) Sacro-iliac disorders	
(4) Vascular insufficiency	(Intermittent claudication involving the sacrospinales or gluteal muscles.)

Disc degeneration can give rise to symptoms by allowing postural changes to occur, by producing an unstable spinal segment, and by virtue of its association with subluxation of the posterior joints and with posterior joint arthritis.[1] Postural changes have been included because it can be shown by experiment that the disc itself is the main factor checking movement between adjacent spinal segments (Fig. 1 a and b). Excessive movements and abnormal postures can only occur once the annulus has lost some of its elasticity.

TABLE III.

FACTORS PREDISPOSING TO HYPEREXTENSION OF THE LUMBAR SPINE

1. Lax abdominal muscles—	Age Repeated pregnancies Abdominal operations
2. Obesity	
3. Pregnancy	
4. Tight anterior capsule of hip joint	
5. High heels	
6. Subluxation of posterior joints	

One of the commonest postural changes seen in everyday clinical practice is hyperextension of the lumbar spine. There are many predisposing factors (Table III). As the postural changes must

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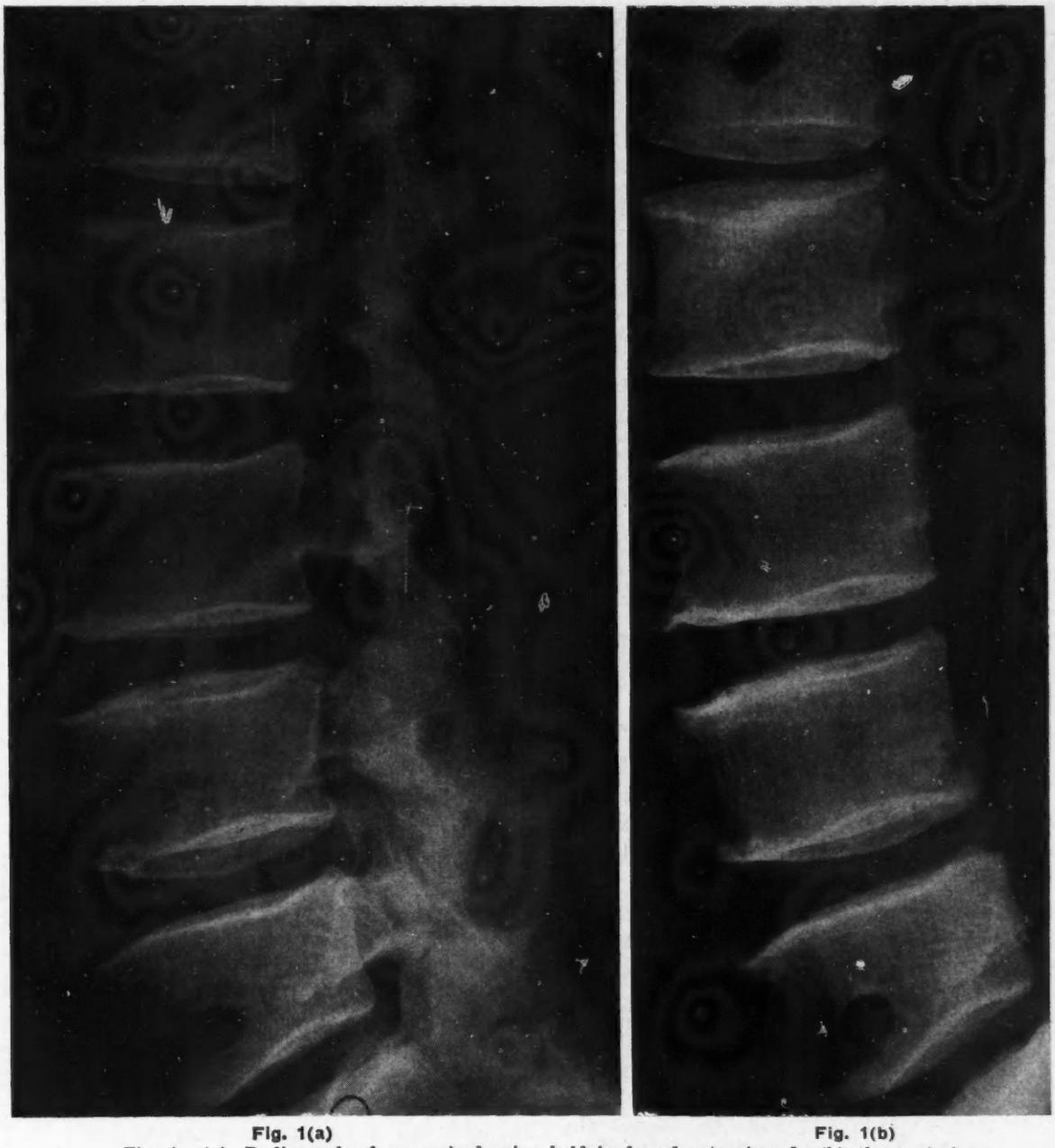

Fig. 1(a) Fig. 1(b)

Fig. 1.—(a). Radiograph of an excised spine held in forced extension. In (b) the posterior arches have been removed and the same force has been applied. Note that although some disc degeneration is present there is no increase in the amount of extension obtained. The factor limiting movement therefore (within the range set by the experimental conditions) must be the disc and not the posterior arch structures.

be preceded by some loss of annular elasticity, the number of segments involved is variable. The whole lumbar spine may be involved, producing a hyperlordosis, or the change may be confined to the lumbo-sacral segment. Whatever the extent, the mechanism of production of symptoms is the same. The posterior joints are constantly held at the extreme of their extension range. Subluxation of the posterior joints may also give rise to segmental hyperextension. As the intervertebral discs lose height, the posterior joints tend to subluxate (Fig. 2), the dorsal capsule stretches and eventually the tip of the inferior articular facet impinges on the lamina below. When this occurs, the joints are lying in the position they adopt on extreme extension. It is important to realize that posterior joint subluxation is not a rare pathological curiosity—it is, in fact, a common post-mortem finding in spines showing marked degenerative changes in the disc.

In both these conditions then—static hyperextension and subluxation of the posterior joints —any extension movement must strain the al-

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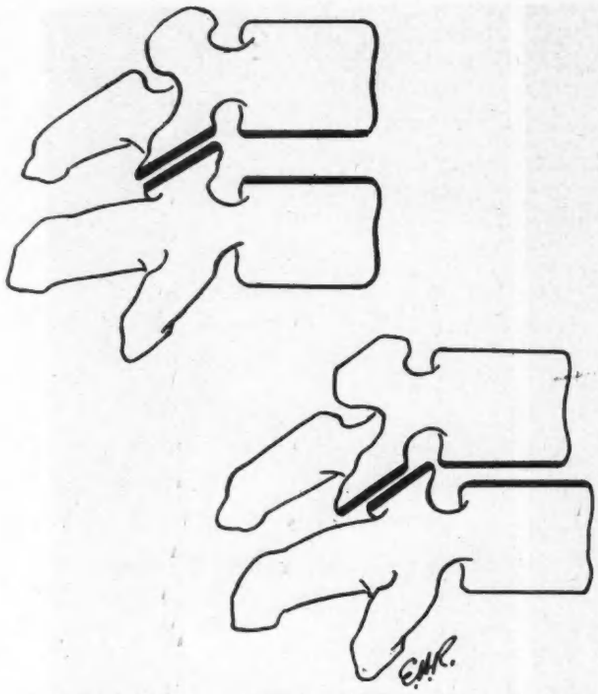

Fig. 2.—Diagram to show how loss of disc height leads to subluxation of the posterior joints.

ready extended joints. Lloyd drew a good analogy with the wrist. A blow applied to the wrist when it is held in the neutral position is not painful because most of the force of the blow is absorbed in the movement that occurs. The same blow applied with the wrist held in full dorsiflexion is painful as there is no safety factor in movement. Likewise, with the hyperextended back, there is no safety factor of movement, and extension strains are painful.

Extension strains and activities tending to increase the lumbar curve are very common in everyday life: sitting with the legs out straight, getting up from the sitting position, carrying weights above waist level, reaching above the level of the shoulders, or lying face down. After prolonged standing, the back sags and the lumbar curve is increased. When there is postural hyperextension of the lumbar spine, the lumbar curve is never completely obliterated on forward flexion. In such activities as prolonged stooping or stooping forward to pick up a weighty object from the floor, the powerful contraction of the sacrospinales acts like a bowstring increasing the curve and forcing the joints into hyperextension (Fig. 3).

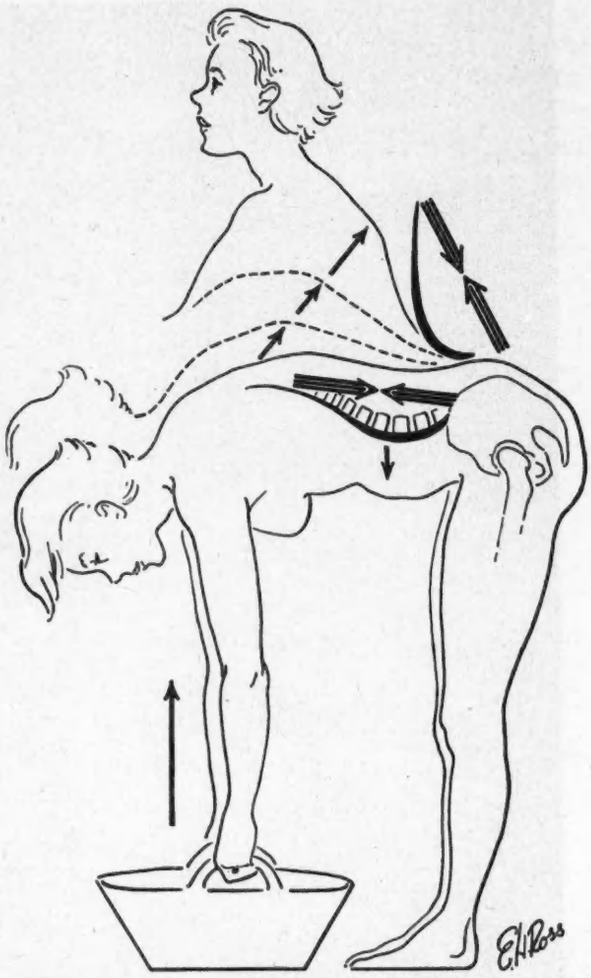

Fig. 3.—Diagram to show how the sacrospinalis may act as a bowstring, increasing the lumbar curve when the patient stoops forward with the knees straight to pick up a weighty object from the floor.

CLINICAL PICTURE

The patient complains of pain over the lumbosacral region. The pain may be referred to both buttocks, and on occasions may be referred down the back of the thigh, but is not experienced in the calf. Pain radiating down the back of the leg as far as the calf is much more likely to be due to nerve root irritation than a referred pain.

The symptoms may develop gradually, or they may come on suddenly as the result of a forced extension strain. The pain is aggravated by any activity that puts an extension strain on the back, such as lifting the baby out of the play pen, pushing up windows, prolonged stooping as in bedmaking or washing the hair over a basin. The pain is relieved by putting the spine in flexion—sitting with the knees higher than the hips, flexing the knees on to the chest, or lying on the side with the knees bent up.

On examination, the increase in the lumbar curve will be clinically apparent only if it involves the whole lumbar spine. During acute attacks of pain, all movements are limited be-

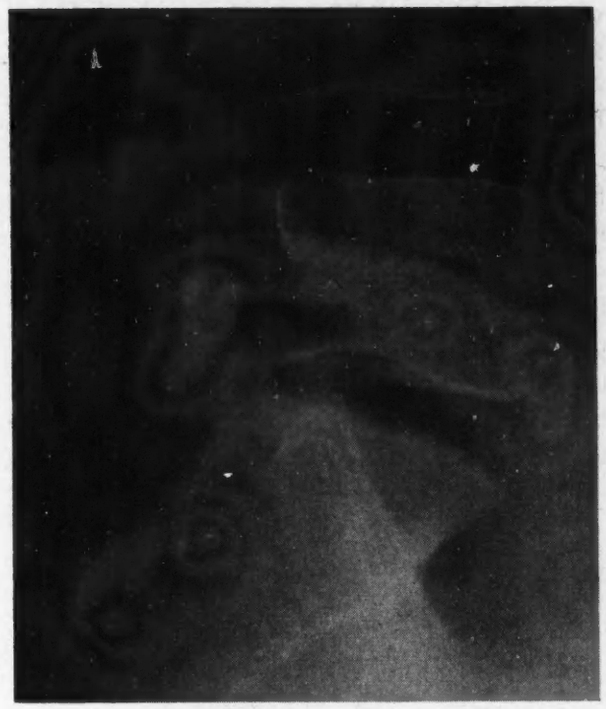

Fig. 4.—Lateral view of the lumbar spine. At the L4/5 segment, if a line drawn touching the under surface of the body of the 4th lumbar vertebra is extended posteriorly, it will cut through the tip of the superior articular facet of L4. This is the normal anatomical position. In extreme subluxation the tip of the superior articular facet will seem to impinge against the pedicle above. At the lumbosacral level in this patient the "vertebral body line" extended posteriorly cuts through the superior articular facet of the sacrum well below the tip. There is a slight degree of subluxation at this level.

Fig. 5.—Antero-posterior view of lumbar spine, showing subluxation of the 4/5 facet on the right. The inferior articular facet of L4 is over-riding and the tip of the facet is impinging on the lamina below. At the site of impingement there is a reactive bone sclerosis.

cause of muscle spasm, but otherwise the flexion range of movement is fair. Extension is limited. If the patient is examined while the examiner places a finger on the anterior and posterior iliac spines, it will be seen that, shortly after extension of the spine is attempted, the patient rotates the pelvis. True extension of the spine is the amount possible without rotating the pelvis. Forced extension and rotation of the spine are painful.

If the patient is in pain at the time of examination, lying flat on the examining table is not comfortable, and patients are more comfortable if they bend their knees and hips. Straight leg raising may be within normal range, but if the patient raises both legs, actively holding the knees out straight, he experiences pain in the back.

The abdominal muscles are frequently weak; many patients are obese and some have limitation of extension of the hips.

Radiographs do not usually show the hyperextended position of the lumbar spine unless they are taken with the patient standing. Subluxation of the posterior joints can be recognized by careful analysis of good-quality radiographs (Figs. 4, 5 and 6). Analysis of the posterior joints between the fifth lumbar vertebra and the sacrum is difficult on radiographs because, unlike

Fig. 6.—Oblique view of the lumbar spine—there is a marked over-riding of the facets at the L4/5 joint. The articular surfaces show only 50% apposition.

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the intervertebral foramina above this level, which face directly laterally, the intervertebral foramina at this level face forward and laterally, with the result that there is overlapping of the outline of the facets, due to rotation.

TREATMENT

Rest.—As for treatment, the key word is flexion. During the acute severe attack of pain the patient should be nursed in bed in a flexed position (semi-Fowler). This is most easily achieved by putting a small wooden crate under the mattress at the foot of the bed and a rolled up blanket or another box under the mattress at the head of the bed (Fig. 7). The buttocks should rest on the part of the mattress that is beginning to slope up towards the raised lower end of the bed. Ideally, bed rest should be complete and the patients should remain in bed until they have been able to move around in bed without pain for one week.

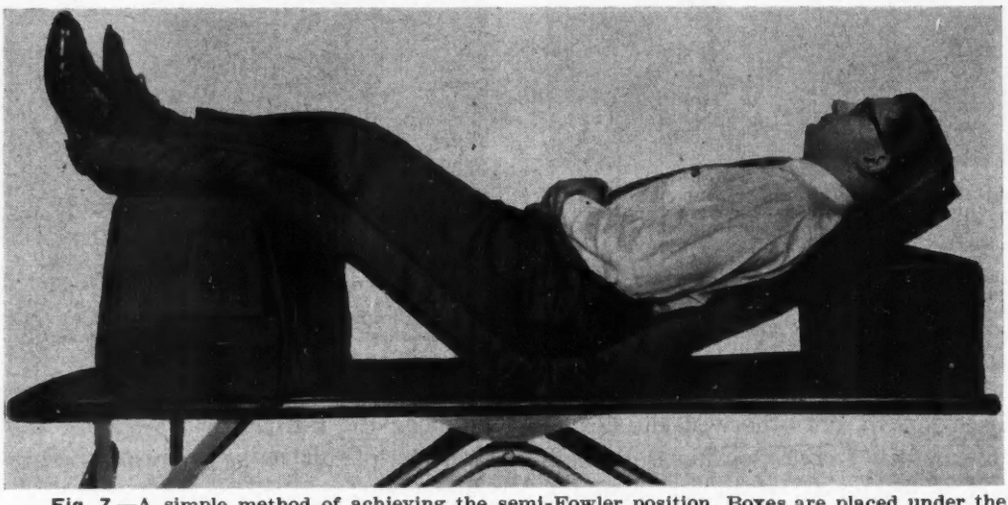

Fig. 7.—A simple method of achieving the semi-Fowler position. Boxes are placed under the mattress at the head and foot of the bed. It is important that the patient's buttocks should lie on the "upslope" of the mattress.

If bed rest of this order is economically impossible, the patient can be provided, as a second best alternative, with a plaster jacket. This should be applied with the patient standing, holding the lumbar spine slightly flexed.

Exercises.—When the pain has subsided the patient should be given exercises designed to build up the strength of the gluteal and abdominal muscles in an attempt to decrease the lumbar curve. All the abdominal exercises should be performed with the hips and knees flexed. Straight leg raising—though it exercises the abdominal muscles—increases the lumbar curve and aggravates the patient's symptoms. The exercises should be supplemented with forced passive flexion of the spine which the patient can do himself. On no account should the patient have hyperextension exercises.

This is the group of back pains that is sometimes dramatically relieved by a flexion and rotation manipulation.

Flexion routine.—No amount of exercising will help these patients if they continue to strain their backs during daily activities. One of the most important aspects of treatment is re-education. The patients must be shown how to rest their backs, and how to avoid repeated extension strains. Each patient presents an individual problem, but in general the following points are of importance.

Sleeping.—A board should be placed underneath the mattress to prevent it from sagging; the patient should sleep on the side with the hips and knees flexed; he should never sleep face down. If the back is painful and stiff on arising, the patient should arrange to get up fifteen minutes earlier and lie on the floor for fifteen minutes, with the spine fully flexed. A pillow should be placed under the shoulders, the knees flexed up on to the chest and supported in this position by placing the soles of the feet against a chair. Alternatively, the patient can lie in a bath of hot water, holding the knees against the chest.

Standing.—The patient should learn to stand with the stomach "pulled in," and the lumbar spine straight. (Getting the patient to practise standing with his back flat against a wall, with

the back of his heels touching the wall as well, will help him to adopt this posture.) After prolonged standing, the spine tends to "sag," the lumbar curve increases, and this gives rise to pain. When standing for any length of time, the patient should place one foot on a low footstool. This flattens the lumbar curve. High-heeled shoes increase the lumbar curve and should be discarded.

Sitting.—The most comfortable way for these patients to sit is with the knees higher than the hips—as when the feet are placed on a footstool or as when sitting with the knees crossed. The chair should have a firm seat and back, and the seat should be no higher and no lower than the distance from the patient's knee to the sole of his foot. Patients should never sit with the legs out straight, as this posture increases the lumbar curve. This is important when driving. It is better to pull the car seat forward as far as possible, so that the knees are flexed.

Housework.—The repeated stooping and lifting inherent in housework makes it a very "back-aching" task. Housewives must be told that all their cleaning equipment should have long handles, and that they must not stoop forward when using them. They must not carry heavy loads in the laundry basket, and they must avoid reaching up when putting the clothes on the clothesline. If they stand to iron or stand for any length of time at the sink, they should keep one foot on a low footstool. The kitchen should be so arranged that articles in daily use are stored on shelves at shoulder level. It is important to teach housewives how to lift, keeping the back straight, and they should be warned not to carry anything heavy above waist level. Beds should be pulled away from the wall so that the housewife can walk around them, and sheets should be tucked in with the patient squatting with the spine straight.

In summary, these patients should sit down whenever they can, and sit with their knees higher than their hips. They should avoid heavy lifting, reaching and stooping. They should not get overtired, and they must not get overweight. The obese must make every endeavour to lose weight; it is almost impossible to stop back pain in a patient who is overweight and who has a hyperextended spine.

Corsets and braces.—The majority of patients seen early will show a gratifying alleviation of symptoms on the simple routine of rest, exercises, and guarded activities. If the symptoms have been of long duration, some patients will require, in addition, support for the back. On the whole, it is better to supply corsets for women and braces for men. The corsets should be long, coming down to the level of the great trochanters. They should be reinforced with four

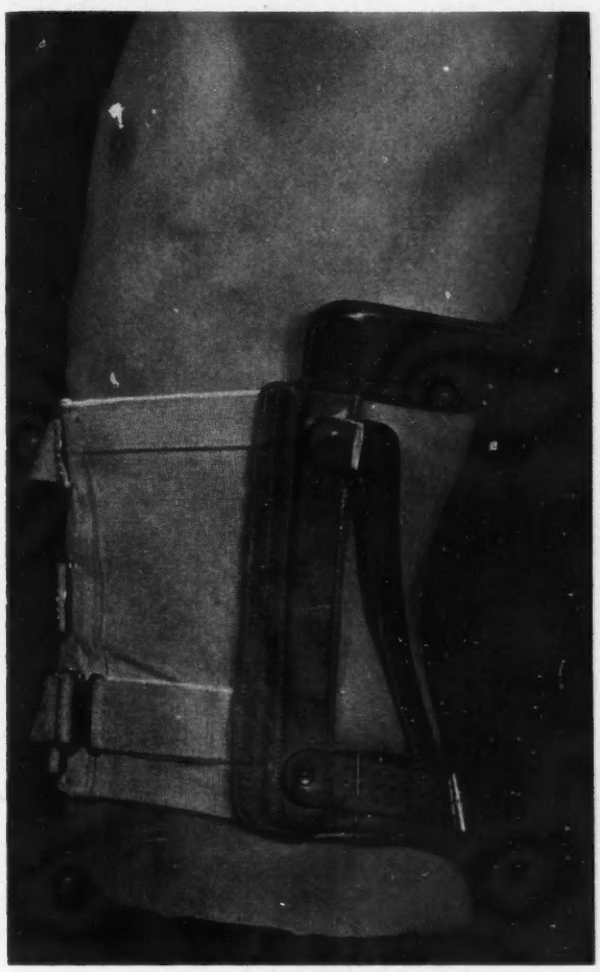

Fig. 8.—The Williams flexion brace.

rigid posterior steels. These steels should not curve to fit the spine, but should run in a straight line from the thorax to the sacrum, so that when the front of the corset is tightened up the spine will be flattened against the steels. If this point is not observed, the corset will tend to hold the spine in the position of deformity and perpetuate the symptoms.

For men, the Williams flexion brace is ideal (Fig. 8); by virtue of its hinge arrangement, the brace tends to flatten the lumbar curve, prevents it from being forced into hypertension on lifting, and, at the same time, gives sufficient support to guard against unexpected strains.

SUMMARY

One common type of low back pain is brought on by hyperextension of part or all of the lumbar spine. It is commonly seen during and following pregnancy, and in the 35-45-year age group, in people of increasing weight and decreasing tone of abdominal muscles. The pain is situated over the lumbo-sacral region, but on occasion may radiate down the back of the thigh. The symptoms are aggravated by extension strains, and are relieved by flexing the spine.

Treatment is conservative, and consists of rest in the initial phases, followed by exercises designed to mobilize the lumbar spine and decrease the lumbar curve. An important aspect of treatment is the instructions given to the patients showing them how to guard against extension strains. Some patients require a back support in addition, and this should be so designed that it tends to flatten the lumbar spine.

The study of the pathological changes in the lumbar spine which forms the basis for the clinical aspect of this article, was made possible by a grant from the National Research Council of Canada.

The research has been conducted over the last four years under the direction of Dr. R. I. Harris, and with the assistance of Dr. R. M. Harrison, Dr. C. Laurin and Dr. C. Menard. The author would also like to acknowledge his indebtedness to the Medical Art Department and the Medical Photographic Department of the Toronto General Hospital for the illustrations.

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MENINGITIS DUE TO LEPTOSPIRA CANICOLA: FIRST REPORT OF OCCURRENCE IN CANADA*

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CANICOLA FEVER or leptospirosis canicolaris is still a rare disease. Although there is an abundance of literature on Weil's disease or leptospirosis icterohæmorrhagiæ, there is a paucity of written material on canicola fever. Consequently, it was felt advisable to present this case which is believed to represent the first known occurrence of this disease in Canada.

In 1931, Klarenbeek and Schüffner[1] isolated and serologically identified a leptospiral strain different from previously described species. The first human case in the United States was reported by Meyer and his associates[2] in 1938. From a review of the world literature, Minkenhof[3] in 1948 compiled 98 cases to which he added 7 other cases. Our own review of literature[4-8, 17, 18] from 1948 to 1952 permitted the addition of 17 more cases including ours, making a total of 124 cases. These cases are distributed as follows: Holland, 49; Denmark, 21; Switzerland, 18; United States, 10; Germany, 6; England, 6; France, 5; China, 2; Australia, 2; and Austria, Norway, Argentina and Canada 1 each.

Since Canadian medical literature is devoid of reference to canicola fever, we present this case with a discussion of pathogenic, laboratory and epidemiological aspects. These features should be of interest to the medical, veterinary and hygiene professions.

On January 5, 1953, J.E., a 25-year-old male, was admitted to Pasteur Hospital, complaining of generalized aching, most pronounced in the neck and in the back. The onset, seven or eight days previously, was marked by loss of consciousness, headache, chills, dizziness and slight stiffness of the neck. Questioning about animal contacts revealed that he had been bitten on the hand three weeks before by a neighbour's dog. As the wound became infected, he received a week later a prophylactic dose of antitetanus serum. This injection was apparently not well tolerated since hypersensitivity signs such as urticaria, chills and arthralgia appeared soon afterwards. As the symptoms were becoming gradually worse, with involvement of the central nervous system, his physician requested hospitalization with a diagnosis of tetanus or rabies.

Physical examination.—On admission, the young man (who was well developed and well nourished) was euphoric and appeared moderately ill. The oral temperature was 101.2° F. with a radial pulse of 78 per minute. No rash or icterus was present. The lungs were clear to auscultation and percussion, and there was no cough or chest pain. The heart was normal in volume and rhythm and no adventitious sounds were heard. Liver and spleen were not palpable. Neurological examination revealed a slight nuchal rigidity, and cutaneous and tendon reflexes were present. Kernig and Romberg signs were noted, while Babinski's reflex was absent. Muscular tonus

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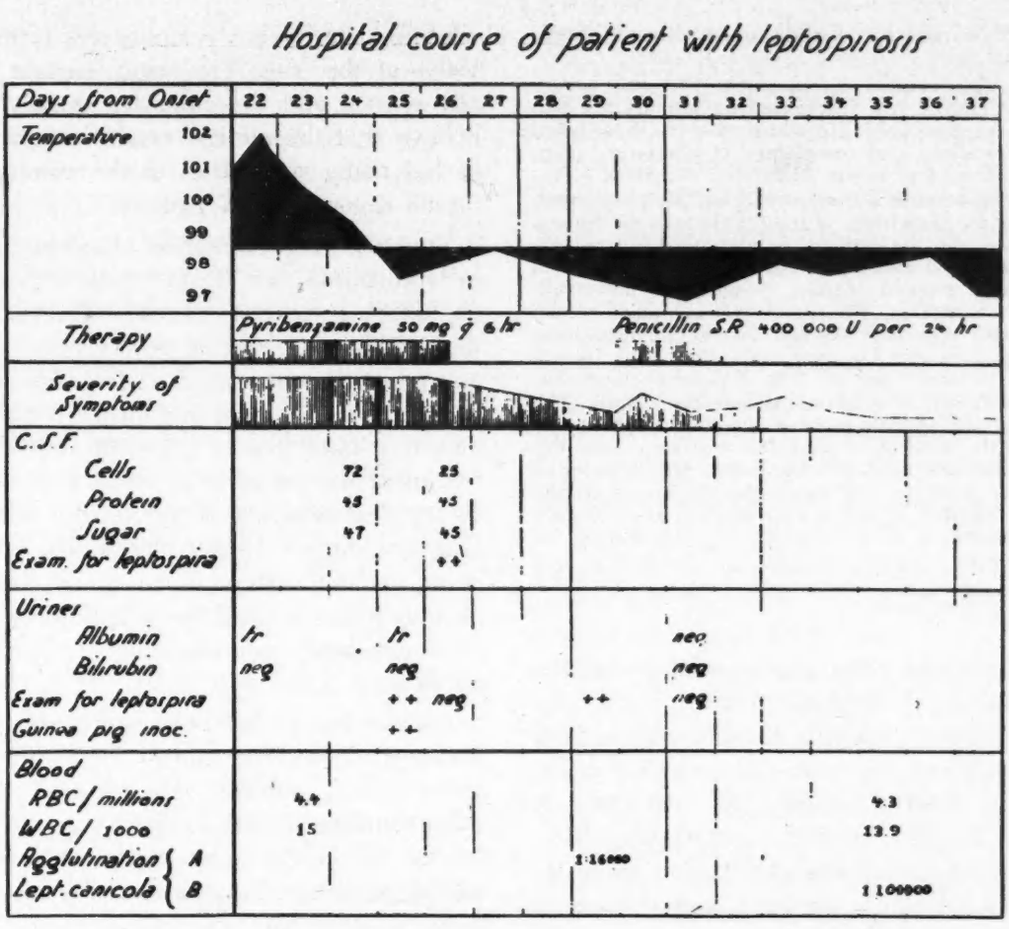

A Agglutination titer determined by the United States Public Health Laboratories.
B Agglutination titer determined by the Pasteur Institute Paris

Fig. 1

and superficial sensation were normal. There was a loss of spatial orientation of voluntary movements. The step was slow and hesitating. Considering the involvement of the posterior columns, the resident made a tentative diagnosis of tabes dorsalis or multiple sclerosis.

Laboratory studies.—The hæmatological picture was as follows: erythrocyte count, 4.5 millions; hæmoglobin value 70%; leukocyte count, 15,000, 61% being neutrophils and 3% eosinophils. Urinalysis consistently showed traces of albumin, few leukocytes and no trace of biliary pigments or bilirubin. No pathogenic organisms could be recovered by blood culture. The Kline exclusion test for syphilis gave a negative result. Spinal-fluid examinations made three days after admission revealed a clear fluid with a pressure of 260 mm., containing 72 cells, 94% being lymphocytes. Sugar content was 47 mg. per 100 c.c., total protein 45 mg. and chlorides 1.46 mg. Löwenstein-Jensen medium inoculated with the sediment was negative after 6 weeks' incubation. The Kolmer complement-fixation test and colloidal gold curve were also negative. Dark-field examination on the 5th day revealed many leptospira-like organisms. Similar examinations of the urine showed spirochætes on the 4th and 6th days and gave negative results on the 5th and 10th days. The organisms observed were actively motile, measuring from 4 to 8μ in length and having from 2 to 5 closely wound spirals. On January 9, a guinea-pig was inoculated intraperitoneally with 2 c.c. of urine. The animal died four days later without evidence of jaundice. The autopsy findings were of a considerable peritoneal exudate and liver abscesses. Dark-field examinations of heart blood and peritoneal fluid showed the presence of many leptospiræ, possibly *Leptospira canicola*. Blood agglutination-lysis tests done in two different laboratories gave positive results for *Lept. canicola*. The first test done 30 days after the onset of disease was reported positive at a titre of 1:16,000 for *Lept. canicola* and negative for *Lept. icterohæmorrhagiæ* and *Lept. pomona*. The second test performed 36 days after the outset was positive at 1:100,000 for *Lept. canicola* and at 1:1,000 for *Lept. icterohæmorrhagiæ*, and negative for *Lept. grippotyphosa*.

Hospital course.—The hospital course is charted graphically in Fig. 1. Under general treatment of bed rest and high caloric diet with supplementary vitamins, the general aching and fever subsided two days after admission. The patient remained afebrile during the remainder of his hospitalization. Since there was a possibility of serum sickness, an antihistaminic was administered during the first four days. With the discovery of leprospira-like organisms in spinal fluid and urine, penicillin (400,000 units per day) was administered from January 14 until the patient's discharge on January 22.

The patient's clinical course was one of gradual improvement. Neurological symptoms were among the first to disappear, although frontal headache disappeared during certain periods to reappear on odd days. The patient was ambulatory by the 10th day and felt well enough to go home. In view of apparent clinical recovery, the pa-

tient was discharged for convalescence at home on the 17th hospital day.

Relapse.—The clinical improvement did not persist long, as the patient was readmitted on January 23, two days after his discharge. He stated that he had fallen twice while walking and complained of abdominal pain, muscular malaise and severe headache. A careful examination of the abdomen did not reveal anything abnormal. To eliminate the possibility of frontal abscess, the fundus was examined and the cranium radiographed but no evidence of increased intracranial pressure was found. An encephalogram showed regular symmetrical and well-pneumatized ventricles. The spinal fluid contained 8 cells and otherwise appeared normal. Blood chemistry was within normal limits. The red cell count and hæmoglobin content were normal. The leukocyte count was never above 8,000, with normal differential counts. The patient remained afebrile most of his stay. First to disappear was the abdominal pain, followed by a slow decrease of muscular pains and headache. After combined penicillin-streptomycin treatment, the patient was discharged as definitely cured on February 21, after 29 days of hospitalization.

COMMENTS

Clinical picture.—The protean nature of the disease and the limited number of cases fully reported make it difficult to offer more than generalities about the characteristics of this infection. The onset is variable. In most cases, it is sudden, marked by high temperature (101-104° F.), pronounced malaise, chills, anorexia, myalgia and arthralgia. In other cases, the onset is insidious with little or no fever, so that the disease can be so mild that the patient does not consult a physician.

Some clinical features such as jaundice, nephritis and meningitis are seen often enough to warrant a brief discussion of each. Jaundice, present in nearly two-thirds of cases of Weil's disease, has been seldom observed in cases reported from the United States. Acute nephritis is also a complication sometimes seen in canicola fever. Although most patients show some mild albuminuria or transient cylindruria, these signs should not be interpreted as evidence of nephritis. In some instances the symptoms are neurological and cases have been reported where the only clinical evidence of disease was that of meningitis. This manifestation was frequently observed by the Dutch workers, who have reported the largest groups of cases.[3, 10] In their series, 20 cases out of a total of 29 presented signs and symptoms of meningitis. Differential diagnosis was from non-paralytic poliomyelitis, mumps meningitis and lymphocytic meningitis. In these cases, spinal fluid was clear, was weakly positive for albumin and contained from 12 to 2,450 cells;[3] at first, neutrophils predominated while in later stages lymphocytes formed 90 to 100% of the cells. The sugar content was usually normal and the chlorides slightly low. We believe that the clinical syndrome observed by us has many similarities to the meningitis syndrome reported from Holland.

Therapy.—The evaluation of antibiotic therapy in leptospirosis is a difficult task because of the variability in severity of the infection and also the tendency to clinical recurrences. When we arrived at a presumptive diagnosis of leptospirosis, penicillin was administered during eight days to a total dose of 3,200,000 units. That this treatment had no curative effect is illustrated by the clinical relapse noticed on the 39th day of illness. Despite intensive treatment with combined penicillin-streptomycin for 26 days, it is to be noted that convalescence was slow and that weakness was pronounced for a considerable period.

A basis for penicillin therapy was Brunner's findings[11] on the experimental infection of hamsters with *L. canicola.* He reported that penicillin significantly lowers death rates in hamsters treated before the outset of the disease, but he added that treated animals usually tended to be carriers. Penicillin was of no value after the appearance of symptoms in the animals. This experience has a parallel in human infections, for, although some relief of symptoms has been reported in early infection, penicillin was of little value if given late in the disease. In a review of eight cases treated with penicillin, Stagg and Leibovitz noted that all but one patient had clinical recurrences. Hall and associates[12] critically appraised the use of chloramphenicol, aureomycin, penicillin, and streptomycin, and concluded that none of these agents was effective in the therapy of leptospirosis. Brunner and Meyer,[13] however, found aureomycin and streptomycin effective in the treatment of clinical canine leptospirosis. Whitehouse in 1952 reported the clinical effectiveness of aureomycin in canicola fever but noted a relapse eight days after cessation of the antibiotic. Stagg and Leibovitz reported in 1951 a dramatic alleviation of symptoms in canicola fever 24 hours after aureomycin therapy and a complete and definitive remission of symptoms within a week. No doubt further trials are warranted before definite conclusions can be drawn concerning the best treatment of leptospirosis.

BACTERIOLOGICAL AND SEROLOGICAL TESTS

Direct examination of blood, cerebrospinal fluid and urine may show leptospiræ. In our case, leptospiræ were observed once in the spinal fluid and twice in the patient's urine. In contrast to Weil's disease, *Lept. canicola* is very seldom found in blood. Because of artefacts such as fibrin strands, protoplasmic extrusions from platelets, and erythrocytes (pseudo-spirochætes), reliance on darkfield examination is hazardous and the diagnosis of leptospirosis should never be made on these findings alone. Other causes of error are the difficulty of observing the organisms when they are few in number and the impossibility of distinguishing between saprophytic and pathogenic leptospiræ in contaminated urine.

Another bacteriological method which we did not use is direct culture of cerebrospinal fluid and blood in Fletcher's semi-solid medium at 30° C., for at least 28 days under reduced oxygen tension. Some authors find this cultural method preferable to animal inoculation.

On account of bacterial contamination, direct culture of urine is not feasible and animal inoculation should be employed. In this case, the intraperitoneal injection of 2 c.c. of urine killed the guinea-pig in four days. Darkfield examination revealed leptospiræ in the heart blood and in the peritoneal fluid. At the same time, however, post-mortem examination of the exudate revealed the presence of *Escherichia coli*. These findings do not invalidate the accepted opinion that the hamster is the animal of choice; death was precipitated by the coli infection. This event, however, did not prevent the invasion of the blood stream by leptospiræ.

Since leptospiræ possess identical morphology, only serological investigation will permit identification of the species concerned. The serological test most extensively used is the agglutination-lysis test of Schüffner. In this reaction, agglutination of leptospiræ by the patient's serum occurs in lower dilutions while lysis of the organisms appears in higher dilutions. Results obtained from the United States Public Health Laboratories were expressed in agglutination titres and those from the Pasteur Institute, Paris, in lysis titres. Methods using live antigens are considered far more sensitive than those using dead organisms. False positives are rarely seen. Single serum examinations may be considered of diagnostic significance with a titre of 1:400 or more. Negative agglutination tests 30 days after the onset of illness rule out the infection. Antibodies against *L. canicola* usually appear on the 10th day, reach a maximum on the 30th day and can remain elevated for many years. For the diagnosis of leptospirosis it is important, if the variety is to be known, to include such antigens as *L. icterohæmorrhagiæ, L. canicola, L. pomona, L. grippo-typhosa* or any other species commonly encountered in the country where the agglutination tests are performed. Unfortunately, no commercial antigens are available that give consistently dependable results, so that investigators have to prepare their own antigens. A more generalized use of this serological test in diseases of obscure etiology would undoubtedly permit the diagnosis of unsuspected leptospiral infections.

Source of infection.—In approximately 50% of cases, it has been possible to trace back the source of infection to contamination with dog's urine. In this report, a dog was also found responsible for transmitting the infection by means of its salivary glands. As often happens, the dog was killed by the police soon after the biting episode, and no serological examination could be made. Fortunately, however, the dog's head was kept in the frozen state, and the examination of salivary gland extracts revealed the presence of leptospira-like organisms. The peculiar sniffing habits of these animals make understandable leptospiral infections of their salivary glands. The incubation period is unknown, but appears to be one or two weeks. In the case reported, the incubation time was approximately one week. No transmission from man to man has ever been observed. Until now, only the dog has been found to be a reservoir of *L. canicola*. This animal can also be infected with *L. icterohæmorrhagiæ*.

Leptospirosis due to *L. canicola* is a common and serious disease in dogs. Two clinical entities are mainly encountered: dog typhus ("the yellows"), characterized by jaundice and considerable hepatic damage; and Stuttgart disease, characterized by hæmorrhagic gastroenteritis without jaundice. The dogs usually die of uræmia and the mortality rate is 50 to 80%. Some mild forms must certainly exist if we consider the high percentage of dogs serologically positive for *L. canicola*.

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Generally speaking, the serum titre in between 4 and 15% of dogs is 1 in 300 or more against *L. canicola;* in dogs over 6 years of age, this percentage has been found to be 90%. Meyer[16] found 25% of dogs positive in Northern California and 19% in Southern California. Raven[19] reported that 38% in Pennsylvania were or had been infected. In Canada, no such surveys have been carried out, but it can be expected that such a situation may exist.

The number of human infections due to *L. canicola* is very small if compared with those reported for *L. icterohæmorrhagiæ*. This situation can be partly explained if we accept that infected rats shed *L. icterohæmorrhagiæ* for the rest of their lives whereas dogs infected with *L. canicola* are transient shedders of the organisms. Serological surveys have shown that in some instances 50% of rat-catchers or fish-workers were positive to *L. icterohæmorrhagiæ*, whereas persons in close contact with dogs did not possess antibodies against *L. canicola.*

SUMMARY

A case of leptospirosis due to *Leptospira canicola* with the clinical picture of meningitis is presented. This is believed to be the first case reported in Canada. The source of infection could be traced to an infected dog. Penicillin therapy did not show definite antileptospiral activity since a clinical relapse was experienced. Emphasis is placed on the importance of development of antibodies in the serum for the diagnosis of the disease. As more agglutination tests for *L. canicola* are done in conditions of obscure etiology, this infection will probably be found to be more frequent in Canada than heretofore believed.

We are indebted to Dr. Martha K. Ward of the United States Public Health Laboratories, Chamblee, Georgia, and Dr. B. Kalochine of the Pasteur Institute, Paris, for performing leptospiral agglutination-lysis tests.

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PRIMARY SYSTEMIC AMYLOIDOSIS

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AMYLOIDOSIS is a storage disease of unknown cause in which a mucopolysaccharide protein complex is deposited in the tissues. Grossly the involved organs are firm, translucent and waxy. In routine microscopic sections this material is hyaline and pink-staining. Because it stains blue-black like starch when treated with iodine and dilute sulphuric acid, Virchow called the material "amyloid" and the disease amyloidosis. It is classified into several types on the basis of staining qualities, distribution and the presence or absence of a predisposing disease. The possibility that there is more than one amyloid is suggested by the varying staining qualities and chemical properties.

PATHOGENESIS

This rare entity has been considered the result of disordered antigen-antibody response. The frequent association of bone marrow plasmacytosis lends support to this thesis. It has been suggested that every case of primary amyloidosis is associated with unrecognized or subsided plasma cell proliferation. It is seen in animals used for the production of antisera, and in those given excessive casein. It is rare in the Orient, where the diet is probably poor in protein. Amyloidosis is thus related in some way to proteins. Hyperglobulinæmia is mentioned but is frequently seen in the predisposing disease, so that its significance is uncertain. The polysaccharides in amyloid are similar to chondroitin sulphuric acid and hence related to hyaluronic acid, a component of collagen tissue. Amyloidosis is therefore associated with the immune response and collagen tissue.

CLASSIFICATION

Classification is unsatisfactory since we are comparing a variety of conditions that may be generalized or focal.[1, 2] The only common factor is an acidophilic hyaline material. At present at least two forms are distinguished—primary and secondary amyloidosis; either may be focal or systemic: (1) Primary amyloidosis—systemic or focal. (2) Secondary amyloidosis—systemic or focal. (3) Amyloidosis secondary to multiple myeloma—systemic or focal.

Since this article deals with primary amyloidosis, the other varieties will be only briefly mentioned.

Secondary amyloidosis is usually associated with a chronic suppurative disease. In hospitals for chronic diseases autopsies of tuberculous patients reveal 25% with this complication.[3] It is seen rarely in rheumatoid arthritis, ulcerative colitis, leprosy, Hodgkin's disease, leukæmia, carcinomatosis and spinal cord injuries. The principal tissues affected are the parenchymal portions of liver, spleen, adrenals and kidneys. The advent of modern chemotherapy and improved surgical techniques has decreased the incidence of the secondary variety. The form found with multiple myeloma is usually listed separately, since in its staining qualities and distribution it tends to resemble primary amyloidosis. Its incidence is about 10-15% of myeloma cases.[4, 5]

Focal cases are very rare. The larynx and trachea are the usual sites of deposition but it does occur in the urinary bladder, heart, small bowel and skin.[6, 7, 8] As most of these focal cases are identified by a study of surgical material, it is possible that all are really systemic forms. Their local character is supported by the finding of large tumour-like masses of amyloid in most instances. Small amounts of amyloid in the seminal vesicles, myocardium and islets of Langerhans are occasional incidental findings in autopsies of elderly people.

PRIMARY AMYLOIDOSIS

Primary systemic amyloidosis[1, 9, 10] was referred to by Wilks in 1856. Thirty years later it was first adequately described by Wild as a form of lardaceous disease in which the deposition occurs mainly in the heart and other mesodermal organs. It is rare, only about 100 cases having been reported in the world literature. This form is characterized by the absence of predisposing disease. According to Dahlin this is the only essential feature, although the deposits usually stain atypically and the distribution tends to differ from that of secondary amyloidosis.

In the primary form, amyloid is always present in the small blood vessels throughout the body. It is usually present in the heart and frequently in the gastrointestinal tract, tongue, skeletal muscle and skin. The liver, spleen, kidneys and adrenals are extensively involved in over one-third of the cases. Patients with the primary form are usually over 50 while the secondary variety is more commonly seen in young adults. Often the only distinguishing feature is the failure to find a predisposing disease, so primary systemic amyloidosis is not a clear-cut entity.[11, 12]

SYMPTOMS AND SIGNS

The symptoms and signs depend on the sites affected and the extent of the amyloid infiltration.[13] Since these are extremely variable, the protean nature of the clinical manifestations is readily explained.

Weakness and weight loss occur early. Some of the weakness is probably due to replacement of muscle cells by amyloid or perhaps the result of interference with the arterial circulation. The tongue is involved in about half the cases, resulting in a smooth, firm macroglossia in one-third.[14] It usually becomes striking if present and eventually may cause marked dysphagia. Dryness of the mouth arises when the salivary glands are much involved.

The heart contains amyloid in over 80% of the cases.[6, 15] Cardiac enlargement and myocardial insufficiency frequently follow. The electrocardiographic changes are non-specific: low voltage, diphasic or low T waves and occasionally prolonged P-R intervals or other conduction disturbances. About one-half the patients with the primary systemic form die as a result of cardiac failure.

About 60% of the cases have involvement of the gastrointestinal tract.[16, 17] This is seen particularly in the muscularis and mucosal blood vessels of the stomach and small bowel. In several instances it has resulted in ulceration and fatal hæmorrhage. Dysphagia, anorexia and diarrhœa are not infrequent. Rarely, severe constipation or complete obstruction may result from the "focal tumours."

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Amyloidosis of the skin may be focal or diffuse.[18] It occurs in roughly 25%. The commonest lesions are purpura and ecchymoses. The latter are notable in skin folds about the eyes, breasts and thighs. The purpuric lesions clear rapidly but often recur and, as no disturbance in platelet function is demonstrable, the diagnosis of allergic purpura is often made. These lesions are probably the result of infiltration of the blood vessels. Cryoglobulinæmia has not been implicated as a cause of the purpura but should be tested for in future cases. The skin may also have translucent papules or nodules, or a rare diffuse involvement called "scleroderma amyloidosum."

Pulmonary deposits are usually confined to the small blood vessels and no clinical signs occur in most instances, but there are at least four cases of chronic cor pulmonale attributed to lung involvement. Laryngeal thickening or the more rare tumour-like deposits often result in hoarseness.

Liver infiltration is manifested by enlargement.[19, 20, 21] Jaundice is very rarely seen and hepatic insufficiency almost never supervenes. Clinical signs are unusual apart from generalized wasting, anorexia and indigestion. Spider angiomata are very rare, despite extensive involvement. Results of liver function tests are normal, but decreased bromsulfalein excretion and diminished total blood protein may occur late in the course of the disease. Little is known about the various globulin components. Portal hypertension has not been mentioned except for one case with œsophageal varices and hæmorrhage.

The spleen is seldom palpable and never produces symptoms unless it ruptures.[22] The kidneys are least able to withstand the amyloid infiltration, possibly because the glomeruli and small vessels are primarily affected. Proteinuria is the first clinical sign and the globulin content is high, resulting in a urinary albumin-globulin ratio of less than 5. The nephrotic syndrome has been described. Hæmaturia is mild and occasional. The blood pressure is rarely affected despite the widespread arteriolar deposits. It is elevated in less than 20%, and in view of the age group concerned this is easily explained. Occasionally death is due to renal failure.

Little is known about central nervous system involvement but a peripheral neuropathy may result when the vasa nervorum are affected. About six cases have been described with diminished deep reflexes and various sensory changes.[23, 24] Pulmonary abnormalities, impotence and difficulty of micturition have been attributed to autonomic nervous system disease.

The adrenal cortex is infiltrated in 20% of the primary cases but obvious insufficiency rarely results.[25, 26] This is likewise true of the secondary type, where about 90% are extensively involved. Diffuse hard thyroid enlargement due to amyloid[27] may not be suspected until diminished bleeding is noted during thyroidectomy or a needle biopsy is obtained. Over 25% of cases of the primary form have such involvement. Tracheal obstruction can occur as a result of pressure. Hypothyroidism has been reported only once;[28] perhaps the lack of radioiodine studies has led to the idea that it is usually absent. The pituitary gland was involved in one instance, with a picture suggestive of acromegaly and a nonspecific myopathy.[27] While slight infiltration of the pancreas often occurs, only one case of diabetes attributed to primary amyloidosis has been reported.[29] Pancreatic insufficiency is rarely mentioned.

Marrow aspiration has revealed amyloid in routine preparations.[30] When the usual method gives negative results, examination of particle smears is said to disclose amyloid and increased numbers or clumps of plasmacytes. Leukocytes containing engulfed amyloid may superficially resemble L.E. cells. The marrow invasion can result in pathological fractures, but leukopenia and anæmia occur late if at all. When the joints are involved, stiffness and swelling is a presenting feature.

DIAGNOSIS

Primary systemic amyloidosis is a diagnosis requiring confirmation by biopsy. Liver, gingiva, lymph nodes, skin, and tongue are the common sites examined.[31] The diagnosis is proved by autopsy. In the Congo red test a positive result implies removal of over 90% of the dye from the blood in one hour;[32] the test is very seldom positive in primary amyloidosis.

The average life expectancy after the onset of symptoms is about two years, but it may range from a few months to over a decade. There is no specific treatment.[13]

CASE 1

A 69-year-old farmer's wife was admitted to the Ottawa Civic Hospital on April 6, 1954, complaining of progressive weakness, nausea and vomiting of approximately nine months' duration. Her debilitated status precluded an accurate detailed history but any previous

illness was denied. Two weeks of nausea and vomiting while confined to bed finally induced her to come to hospital.

She was cachectic and dehydrated, with a coarse inelastic, thickened, sallow skin. She had a peculiar husky voice. The tongue was enlarged to about twice its normal size. It was rather firm, with atrophic papillæ and some transverse fissuring. The thyroid was easily palpable, slightly enlarged and firm. The cardiac apex was 9 cm. from the midsternal line in the fifth interspace. There was an apical systolic murmur of Grade III intensity that radiated to the base. The pulmonic second sound was accentuated. The neck veins were prominent and filled from below. A smooth, firm liver edge extended across the abdomen at the level of the navel about five fingerbreadths below the costal margin. The spleen and the kidneys were not felt. Pitting œdema was noted in the lower extremities and over the sacrum. The deep reflexes were decreased in the upper limbs and absent in the lower limbs, but peripheral sensation was apparently intact. Vibration sense was equivocal. The left knee was stiff but not swollen and had a diminished range of movement. Other joints were not remarkable.

Results of laboratory studies were as follows: sedimentation rate 13; hæmatocrit 32; hæmoglobin value 10 g.; erythrocytes 3.7 million; leukocytes 6,500; differential blood smear normal; bleeding, clotting and clot retraction times normal; prothrombin time 16 seconds, control 12 seconds; blood Wassermann reaction negative; NPN 176 decreasing to 97: creatinine 4.5 increasing to 5.7 mg.: serum Ca and P normal. Total bilirubin 0.36 mg. and later 0.96 mg. Bromsulfalein excretion test revealed 35% retention in 5 minutes and zero in 30 minutes: thymol turbidity and cephalin cholesterol flocculation normal; total protein 6.1 g.; albumin 3.1 g.; globulin 3.0 g.; alpha 0.5; beta 2.0; gamma 0.5. Congo red test: 25% of the dye was absorbed from the blood in one hour. Histamine—fast achlorhydria.

ECG: showed a regular sinus rhythm of 61 with low voltage in the limb leads. The S-T changes were nonspecific with T diphasic in leads 1 and 2. There was a deep S in the right and a tall R in the left chest leads without definite delay in the intrinsicoid deflection, a finding consistent with but not pathognomonic of left ventricular hypertrophy.

Chest radiography revealed moderate cardiac enlargement. Pulmonary congestion and pleural effusion appeared toward the end of her hospital stay. The stomach and duodenum appeared normal, with no retention of barium. Osteoporosis consistent with age was noted.

Hospital course: Despite the usual measures for congestive failure, her condition gradually deteriorated. Orthopnœa and dyspnœa became prominent, with bilateral hydrothorax and neck vein congestion persistent. Liver biopsy shortly after admission revealed large amounts of atypically staining amyloid material. This biopsy together with the negative history, cardiac insufficiency, macroglossia and renal failure rendered the diagnosis of primary systemic amyloidosis almost certain before autopsy. The patient died on May 25, 1954, seven weeks after admission to hospital.

PATHOLOGICAL FEATURES

The thyroid gland weighed 60 g. It was firm, nodular, dark-brown and translucent on section. The heart weight 375 g. The left ventricle measured 2 cm. in thickness and the right ventricle 0.8 cm. in thickness. The myocardium was moderately firm and rubbery with a waxy translucent appearance. Numerous minute, pale, subendocardial streaks were encountered in both atria. The lungs and pancreas were normal. Section of the liver (1,980 g.) and spleen (125 g.) revealed them to be rubbery, firm and waxy. The adrenals combined weighed 14 g. and the kidneys 140 g. each and were likewise extensively involved. The iodine test was strongly positive in each instance.

Microscopically the greatest deposition occurred in the liver, spleen, kidneys and adrenals. The basement membranes, glomerular tufts and material in the lumina of the tubules at times stained positively with Congo red and PAS. The pancreas was extensively involved. The tongue contained moderate amounts of amyloid. In the heart the deposits were most prominent in the subendocardial regions. Patchy infiltration of the thyroid was present. In all these organs the small arteries and arterioles were involved. This was the only abnormality noted in the lungs, ovaries, uterus, bone marrow and lymph nodes. The gastrointestinal tract was not examined. All the sections gave atypical tinctorial reactions for amyloid. There was no evidence of suppurative disease, multiple myeloma or other malignancy.

CASE 2

A 50-year-old white male first consulted a physician in August 1951, complaining of back pain, indigestion and loss of weight of two years' duration. Extensive investigation was negative apart from the presence of smooth, firm hepatomegaly, allegedly present for ten years. Liver biopsy showed extensive amyloid infiltration between cords of intact liver cells and the sinusoids. The material stained poorly with Congo red, atypically with methyl violet and not at all with PAS. He was started on ACTH and cortisone with marked subjective improvement. The Congo red test showed 46% retention of the dye (later 70% and 100%).

In May 1952, a repeat radiograph of the stomach revealed extensive infiltration of the stomach wall with a large filling-defect along the greater curvature. Gastroscopy showed a superficial slough and pale mucosa on the greater curvature. It was felt that the stomach lesion decreased with the use of cortisone. Readmission to the Montreal General Hospital in June 1952 was necessary because of progressive muscular weakness, increasing bulk and softness of the stools and marked postural œdema. The findings on physical examination were unchanged.

The hæmogram was normal. Study of the upper gastrointestinal tract now showed 80% five-hour gastric retention and 5% 24-hour retention of barium. Radiologically the infiltrative lesion of the stomach wall was unchanged. Serum Na 129 mEq/l.: Cl 105 mEq/l.: K 5 mEq/l. A/G ratio 2.07/1.23 rising to 3.45/1.45. Blood urea was 24 mg.

The patient was placed on a high protein, low salt diet. Mercurial diuretics were given for three weeks and 410 g. of albumin intravenously; in ten days his weight fell from 132 to 116 lb. The blood pressure varied between 100/60 and 120/80. He was discharged on the following regimen: cortisone 125 mg. a day in divided doses; thyroid grains i daily; potassium chloride 25%, one teaspoonful t.i.d. a.c.; Gravol suppositories p.r.n.; testosterone propionate 24 mg. i.m. three times a week.

He died on August 8, 1952. Autopsy was done in the Ottawa Civic Hospital.

PATHOLOGICAL FEATURES

Slight pigmentation of the exposed areas and wrinkles of the palms were noted. The finger nails were pitted. Petechiæ were found on the abdomen and lower limbs. The heart, lungs and pancreas appeared normal. About 500 c.c. of clear amber fluid was found in each pleural space and in the peritoneal cavity. The liver weighed 3,190 g., spleen 310 g. and the kidney 275 g. each. All were firm and translucent with extensive diffuse amyloid deposition. The combined adrenal glands weighed 24 g. and were obviously similar. No unusual gross features were encountered in the gastrointestinal tract with the exception of one calcified lymph node which showed no evidence microscopically of any inflammatory change. The central nervous system was not examined.

Microscopically there was extensive amyloid deposition in the adrenals, pancreas, liver, spleen and kidneys. Only small amounts of medullary tissue remained in the adrenals, and here too amyloid was found. The small arteries of the heart, lungs and gastrointestinal tract were also involved. No sections of the stomach were available.

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Scattered small deposits were present in the subendocardial region of the myocardium. As in the previous case, the usual staining procedures produced atypical tinctorial reactions for amyloid.

DISCUSSION

Both patients exhibited the debility and digestive symptoms suggestive of generalized cancer. In both, smooth hepatomegaly was a prominent feature and diagnosis was made by liver biopsy. While liver involvement predominated in the second case, the first was more classical, having cardiac insufficiency, renal failure and enlarged tongue to help point to the diagnosis. In view of the generalized wasting, the tongue was definitely enlarged although some observers doubted this. A tongue biopsy was not done because of the obvious terminal condition of the patient. Death was due to a combination of congestive heart failure and renal insufficiency, since both were marked.

The second case was studied in the Montreal General Hospital, only the autopsy being done at the Ottawa Civic Hospital. The prosector was more impressed with the likelihood of Addison's disease than were the clinicians. The blood pressures were borderline, about 120/70 shortly before death. With nothing but the pigmentation and a single serum sodium determination to add to the very extensive adrenal amyloidosis it is difficult to say whether Addison's disease was present or not. The use of cortisone somewhat obscures this diagnosis. However, a 50% fall in eosinophils after ACTH tends to eliminate such a diagnosis. The digestive symptoms could be interpreted on this basis, but more likely a mild form of sprue developed due to the amyloid in the gastrointestinal tract. This has been reported by others. In this patient extensive amyloid infiltration of the pancreas with pancreatic insufficiency could also have been a contributing factor. The adrenocortical hormone treatment did not produce a dramatic result other than the usual subjective improvement (described in one other case[33]).

The report of these two patients serves to re-emphasize that this disease is probably much more common than the medical literature indicates.[34]

SUMMARY

Two cases of primary systemic amyloidosis diagnosed ante mortem by liver biopsy have been described, together with the pertinent pathological features. The protean clinical picture, the etiology, diagnosis and treatment have been reviewed. One of the cases was treated with cortisone without any obvious benefit apart from euphoria.

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STREPTOCOCCAL INFECTIONS IN HOSPITAL

So much attention has recently been focused on antibiotic-resistant staphylococci as the chief cause of wound infection in hospitals that the role of the hæmolytic streptococcus seems to have been forgotten. Rountree (*Lancet*, 2: 172, 1955) points out that *Streptococcus pyogenes* is by no means completely under control. Between 1950 and 1954 there was an increaseing incidence of hæmolytic streptococcal cross-infection at the Prince Alfred Hospital, Sydney, Australia. There were only 71 cases in 1950-51 but 115 cases in 1953-54; the rise is correlated with an increase in streptococcal throat infections in the staff. Many of the wound infections were associated with infection by a penicillin-resistant staphylococcus, although all the strains of *Strep. pyogenes* were penicillin-sensitive.

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ADRENOCORTICAL ACTIVITY AND REACTIVITY AS MEASURED BY EOSINOPHIL COUNTS*

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THE ACTIVITY and reactivity of the adrenocortical system in schizophrenia has been under investigation for many years, but we still do not know whether the gland is hypoactive or normally active (Fry[1]). Research groups have markedly disagreed with each other's findings. This must mean that many unknown factors influence the data or else that workers either do not adequately control their experiments or fail to report pertinent data. Some of the known variables include the diagnostic categories, the phase or chronicity of the illness (Stevenson, Metcalfe and Hobbs[2]), the shape of the morning diurnal rhythm and the way it is sampled and analyzed (Halberg *et al.*[3]).

Stevenson *et al.*[2] stressed the need for comparing eosinophil changes after test medication (epinephrine, cortisone) against the usual diurnal rhythm for the group. Hoffer[4] reported that the injection of atropine at 9.30 a.m. accentuated the diurnal rhythm of non-schizophrenic individuals but inhibited the schizophrenic rhythm. It is obvious that all comparisons must be based on the morning rhythm in the same way as radioactivity counts are compared with the background count. Since the decrease in eosinophils induced by medication is used to measure adrenocortical activity, it is essential to examine what we mean by the terms "activity" and "reactivity" when referring to the systems which affect the eosinophil rhythm.

ACTIVITY AND REACTIVITY

Activity refers to the absolute rate of secretion of adrenocortical hormones and may be classified as low, normal or high. If we assume an inverse relationship between eosinophil counts and the blood level of circulating steroids (Pincus, Romanoff and Carlo[5]), we may use the absolute count as a measure of activity at the time of sampling. However, it is difficult to select a standard time because of variations in the shape of the diurnal curve between days and between persons; for example, in one person the lowest count may be reached at 8 a.m. and in another at 10 a.m.

We might have valid comparisons by selecting the period of lowest (night) and highest (day) activity, i.e. the highest sleeping count and the lowest morning count. This would mean obtaining the complete diurnal rhythm for each patient and using the highest and lowest points from the curve irrespective of time.

Reactivity, on the other hand, refers to the ability of a system to respond to a stimulus by either an increase or decrease in the rate of secretion. This need not be directly related to the activity. Four systems are possible: (1) high activity and high reactivity; (2) high activity and low reactivity; (3) low activity and high reactivity; (4) low activity and low reactivity. Probably system (1) is rare since a system already functioning at a high rate of activity is inherently less responsive to further increase in activity; for example, it is easier to accelerate a car from 50 to 70 m.p.h. than from 90 to 110 m.p.h.

MEASURING REACTIVITY

In order to determine reactivity we want to know how quickly the system will depart from its steady state when it is subjected to stress. With a constant stress the reactivity will decrease as the activity rises until the reactivity to this particular stress falls to zero. It is, therefore, impossible to determine the reactivity unless we know what the steady state is; our first eosinophil counts must therefore be made at a time when the eosinophil count is at its height in the morning.

Halberg *et al.*[6] have shown how the morning rhythm is susceptible to time of rising. Fig. 1 is a tracing of a normal person rising at 7.30 a.m.

In this diagram the count in the sleeping state is shown by line *ab*. After rising there is a rapid decrease in the count (*bc*), i.e. the reactivity of the system affecting eosinophil counts is high between 6.30 and 8.30 a.m. Between *c* and *d* the activity of the system is high but reactivity is now low and the organism is in balance with its environment. The change *d-e* may be either up or down but in any case is not marked unless other stresses are applied to the system.

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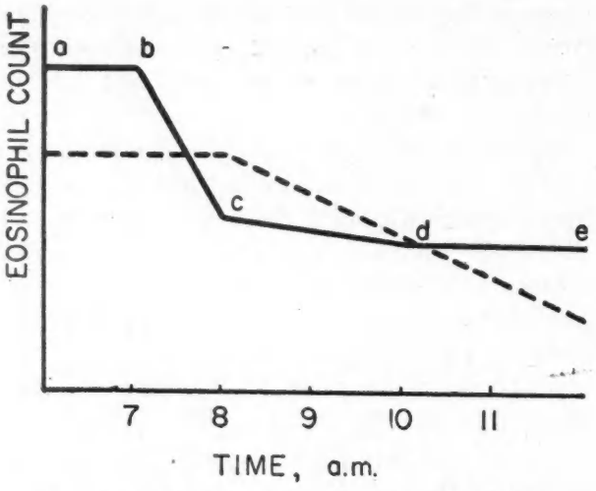

Fig. 1.—Two types of diurnal eosinophil rhythm.

Let us assume that we have a system with a high sleeping activity, that is, a lower eosinophil count and a low reactivity. This can be illustrated by the dotted line in Fig. 1. When this system is stressed it will react sluggishly (low reactivity) but as the stress continues to act it may continue to react at a steady rate. Eventually by 12 noon the decrease in eosinophil count is relatively the same for both systems. However, and this is important, the reactivity of the system immediately after the stress is applied is high in the first example and low in the second one.

Suppose we start our counts at 8 a.m. and continue them to 12 noon as did Stevenson *et al.*,[2] who reported the following counts for a group of catatonics, paranoids and normals (Fig. 2).

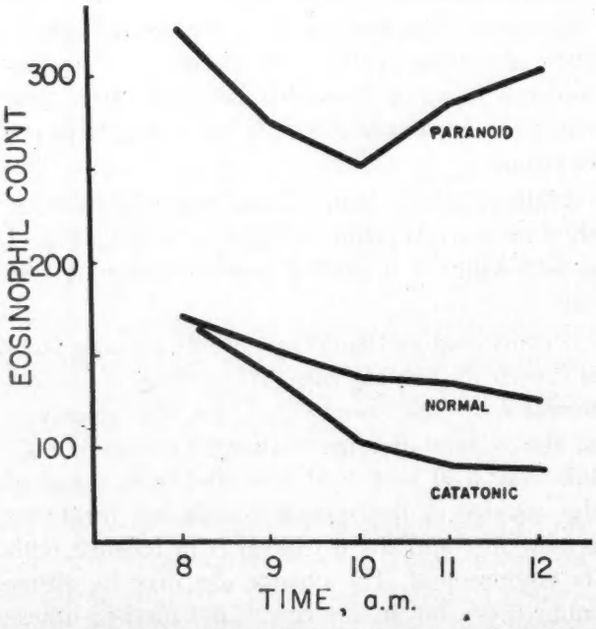

Fig. 2.—Relationship between counts in normals and paranoid and catatonic schizophrenics.

Their conclusions were that the "paranoids show evidence of subnormal activity and response (reactivity) of the adrenocortical system, whereas the catatonics appear to have a moderate hyperactivity or at least a hyperreactivity of this system."

Refer again to the portion of Fig. 1 between 8 a.m. and 12 noon. From it we would conclude that the person whose diurnal rhythm is shown by the dotted line is hyperactive and hyperreactive whereas in reality this system is hyperactive but is *hyporeactive*. Furthermore, the solid line from 8 to 12 appears to be a system characterized by even greater activity and by much less reactivity whereas in reality it is a system characterized by normal or high activity and high reactivity. The point is that we cannot interpret either the activity or reactivity of a system unless we know the highest value of the diurnal rhythm. Referring to Fig. 2 we could, in contrast to Stevenson and his colleagues, conclude that the count in normals and catatonics might follow a curve like the dotted line in Fig. 1 (high or normal activity, low reactivity) with the catatonics less reactive than the normals. The curve in paranoids might be like the solid one in Fig. 1. It is obvious that no conclusions are possible because the excellent research reported in the paper is marred by a lack of eosinophil counts before 8 a.m.

I would suggest that to test reactivity we consider the rate of change in the eosinophil counts for the first three hours following a stress (the descending portion of the curve), whether this stress be morning awakening or administration of epinephrine or cortisone. If two stresses are applied, e.g. epinephrine after awakening, a complete rate curve must be obtained. Unless rates are determined it is impossible to assess properly the reactivity to the test.

The rate data in Table I are taken from the report of Stevenson *et al.*[2]

TABLE I.

RATE OF CHANGE OF EOSINOPHIL COUNT PER HOUR AFTER EPINEPHRINE AND CORTISONE

Time	*Epinephrine*		*Cortisone*	
	Catatonics	*Paranoids*	*Catatonics*	*Paranoids*
8–9.....	39	21	40	40
9–10.....	56	114	39	67
10–11.....	1	–24	24	23
Mean rate.	32	40	34	43

The authors reported that paranoids showed a diminished adrenocortical reactivity whereas the catatonics showed increased reactivity. However, the rates shown in Table I indicate that the paranoids are more reactive than the catatonics. The absolute counts at the lowest point of the diurnal rhythm indicate that the activity of the paranoids is less than the activity of the catatonics. Thus the catatonics have the highest activity and lowest reactivity of the three groups, the normals (orderlies in a mental hospital) come next and the paranoids have the least activity but the highest reactivity. It appears that reactivity is inversely related to activity.

It has been standard practice to report the decrease in eosinophils as a proportion of the pre-injection count; for example, if the initial count is 200 and the final count is 100 there is said to be a 50% decrease in eosinophils and it is assumed that this decrease represents, and is proportional to, a given level of reactivity. This method assumes that the reaction

eosinophils + adrenocortical system $\longrightarrow$

is a first order reaction because only with first order reactions will the rate of change depend primarily on the concentration of the eosinophils. If this were a first order reaction one could obtain a straight line by plotting the log concentration of eosinophils against time. If the reaction is a second order one a straight line is obtained by plotting the reciprocal of the concentration against time. When the data of Stevenson *et al.*[2] are so examined, we find what is apparently a second order reaction for the catatonics and normals. It is impossible to plot the data for paranoids, because too few points on the descending curve are given.

Because the reaction is not of first order there is no justification for using a percentage decrease in eosinophils to measure reactivity. Since we do not know how many factors are operative in the eosinophil rhythm it is much safer to use simple rates of change to express reactivity. Cathcart and Hoffer[7] found that 10 mg. of morphine sulphate injected at 8 a.m. produced changes in eosinophil count as shown in Fig. 3.

Morphine evidently induced little change in the normals and a marked change in the chronic and acute schizophrenics. However, this conclusion is not justified since no data are shown before 8 a.m. and these changes may be chiefly part of the diurnal rhythm of these groups of people. Comparing these data with the observation of Hoffer[4] that there is no change in eosinophil count between 9 a.m. and 1.30 p.m. in normals and a decrease from 200 to 150 in acute schizophrenics, it is obvious that we can conclude that morphine had little action on the diurnal rhythm.

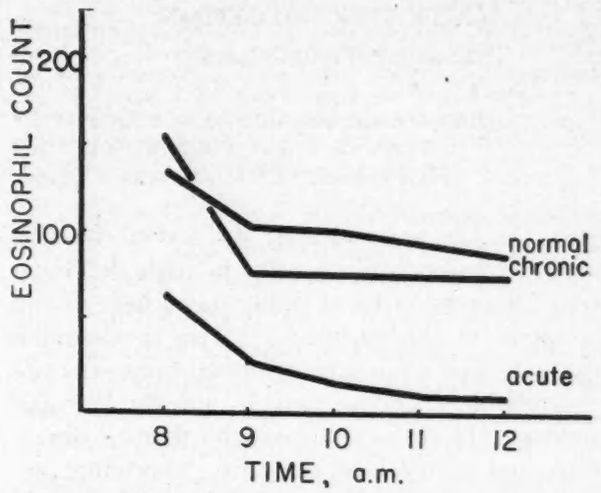

Fig. 3.—Effect of morphine on diurnal rhythm of eosinophil counts of normal subjects and acute and chronic schizophrenics.

The lowest mean counts for normals and chronic and acute schizophrenics were 179, 160, and 101, which would indicate that at the peak of activity the normals were least active and the acute schizophrenics most active, with the chronics in between. It is difficult to assess reactivity but it appears that the acute schizophrenics have the least reactivity and the normals the greatest reactivity, with the chronics in between.

CONCLUSIONS

It is impossible to assay adrenocortical activity and reactivity by means of eosinophil counts unless the total diurnal rhythm is sampled. No valid comparison is possible between groups of subjects unless the activities are compared at a time when the rate is not changing, that is, either at the sleeping eosinophil peak or the wakeful eosinophil trough. The reactivity must be measured by the rate of change of eosinophils.

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ACUTE DEFIBRINATION

REPORT OF THREE CASES

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J. B. DE LEE was probably the first to describe a hæmorrhagic syndrome due to acute defibrination.[1] Numerous recent publications have drawn attention to this problem.[2-18] This syndrome is characterized by sudden, unpredictable and uncontrollable bleeding, which quickly becomes serious. It has been reported after thoracic operations and pathological deliveries, abortions, premature separation of the placenta, amniotic fluid embolism and even after normal deliveries. Some authors have discovered Rh-sensitized women among their cases.[3, 16, 18] The blood lost by hæmorrhage as well as the blood obtained by venipuncture does not coagulate; alternatively, if a clot forms it dissolves instantaneously. Usually the bleeding is localized, but in a few cases a generalized hæmorrhagic syndrome has been observed. Mortality is very high. Revol and Favre-Gilly[15] in a recent survey report 13 deaths in 18 cases. We wish to report three cases of dramatic hæmorrhage due to acute defibrination.

CASE 1

R.P., a boy 14 years of age, was admitted to hospital with vomiting, bowel obstruction and oliguria. Blood pressure was 115/75 mm. Hg. Slight pain on pressure in the umbilical region was noted. Urinalysis revealed slight traces of albumin and hyaline casts. Non-protein nitrogen was 97 mg. per 100 ml. The blood count was normal with 230,000 thrombocytes per c.mm. without any morphological abnormalities or defects of agglutination. A chest radiograph showed a slight degree of opacity suggesting a pneumonitis in the left paracardiac region, and a flat radiograph of the abdomen showed the classical signs of intestinal obstruction. Laparotomy was performed, and a strangulation of the upper third of the small intestine was found. The strangulated part was resected and an end-to-end anastomosis performed. The operation was easy and uneventful. A few minutes after the patient's arrival in the recovery ward the nurse noted a very rapid pulse. Half an hour after the operation, blood oozing from the wound was noticed and the dressing was very soon saturated. The blood did not show any tendency to coagulate and the patient very soon went into acute shock. Blood obtained by venipuncture did not coagulate either. A transfusion of 500 ml. of O, Rh-negative blood was given under pressure and the patient returned to the operating room for reintervention. The abdominal cavity was full of blood. A general oozing was noticed but no special blood vessel could be held responsible. The cavity was cleansed, and fibrin packs as well as topical thrombin applied to the oozing surfaces. About 2,000 c.c. of blood was given during the operation but the oozing kept on, the shock became worse and the patient died on the operating table, the surgeon being unable to stop the bleeding. There was no clot formation in the test tubes 24, 48 and 96 hours after collection. It is to be noted that there was nothing in this patient's past history suggesting a blood dyscrasia. For example, at ten years of age he had undergone tonsillectomy without accident.

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CASE 2

Mrs. L.C., 36 years of age, was delivered on July 10, 1954, of a normal child. In her gynæcological history there was a record of an abortion in 1949 and a normal confinement in 1951, without hæmorrhage. The patient was delivered at 9 a.m. After the delivery, the uterus contracted well and the patient felt well, but an hour later the obstetrician was called because of excessive vaginal bleeding, although the uterus was still very well contracted. An ampoule of Ergotrate was given intramuscularly but the bleeding kept on and the blood showed no tendency to coagulate. The pulse was thready, the blood pressure fell rapidly to 40/20 mm. Hg, the skin was clammy and the patient became unconscious. A blood transfusion was started and the patient returned to the delivery room where the uterine cavity was cleared out. A few pieces of membrane were removed, without any influence on the hæmorrhage. The uterine cavity was packed but this packing was soon saturated and the patient kept on oozing blood *per vaginam*. Three hours after delivery the patient was in a critical state, the pulse imperceptible, the blood pressure nil, auscultation revealing very faint heart sounds. Energetic treatment was instituted. Pressure transfusions and analeptics resuscitated the patient, allowing performance of hysterectomy under spinal anæsthesia. The operation was uneventful. As soon as the two uterine arteries were clamped, oozing in the incision stopped and after the operation blood clots were found in the vagina. The postoperative course was absolutely normal, and two weeks after operation the patient was discharged from the hospital.

This very interesting case has given us the opportunity for a more complete blood study, which enabled us to confirm the validity of the fibrinolytic theory.

BEFORE HYSTERECTOMY

Clotting time: after 4 minutes, a small clot formed but dissolved completely at 5 minutes; 6, 12 and 24 hours later, the blood was absolutely fluid. Calcium clotting time: to 0.2 c.c. of the patient's plasma was added 0.2 c.c. of M/40 $CaCl_2$; no clot formation. Recalcification of 0.2 c.c. of a mixture of 0.9 c.c. of the patient's plasma to 0.1 c.c. of normal plasma gave a clot in 3 minutes. Quick's time: no coagulation. Action of thrombin: to 0.2 c.c. of the patient's plasma 0.05 c.c. (10 units) of a fresh solution of thrombin was added: no coagulation. Fibrinolysin assay: clotting of the mixtures detailed in Table I was observed after recalcification and leaving for 48 hours at 37° C. In the control tubes, 2, 4, 6, and 7, there was absolutely no lysis and the clot remained firm after 36 and 48 hours. On the other hand, complete lysis was observed after 16 hours

TABLE I.

	Patient's plasma (ml.)	*Normal plasma (ml.)*	*NaCl 0.85%*	*At 37° C. after recalcification*
1.	0.04	0.1	——	Complete lysis after 16 hours.
2.	——	0.1	0.04	No lysis after 48 hours.
3.	0.1	0.2	——	Complete lysis after 22 hours.
4.	——	0.2	0.1	No lysis after 48 hours.
5.	0.1	0.3	——	Complete lysis after 48 hours.
6.	——	0.3	0.1	No lysis after 48 hours.
7.	——	0.4	——	No lysis after 48 hours.

at 37° C. in tube 1, after 22 hours in tube 3 and after 48 hours in tube 5.

AFTER HYSTERECTOMY

Clotting time: eight minutes. Quick's time: 13 seconds (control 13 seconds).

COMMENTS

We thus observed that whole blood before the hysterectomy showed only a slight tendency to coagulation. The micro-clot dissolved under our eyes in two minutes with definitive incoagulability. Recalcification of the plasma had no influence on coagulation. The same plasma submitted to the action of a strong solution of thrombin did not clot. This demonstrates that the coagulation defect was caused neither by a deficit of thromboplastic factors nor by a deficit of prothrombin or its accelerators but by the nearly total disappearance of the circulating fibrinogen. The patient's plasma which was added in small quantity (2:7, 1:3, 1:4) to normal plasma was able to dissolve the clots formed after recalcification. That lysis progresses much more slowly *in vitro* than *in vivo* is very difficult to explain but it is a fact admitted by everyone. Normally, one should not observe lysis of a clot in less than 24 hours (at least) at 37° C. Finally, six hours after the end of the episode, normal coagulation was resumed in our case.

CASE 3

Mrs. D.L. was delivered on October 8, 1954, of a normal child. Three hours later she started to bleed profusely. Ergometrin and 500 c.c. of plasma were given. The pulse became thready and the blood pressure fell to 60/40; a transfusion of whole blood was begun and oxygen administered. The hæmorrhage persisted as in the two previous cases, the blood showing no tendency to coagulate. Clotting time study in a tube showed a small clot at three minutes which dissolved immediately and completely at four minutes. One of us (J. de St-V.), called in consultation, made an examination of the uterine cavity. As the examination was negative and the hæmorrhage persistent and becoming worse, hysterectomy was proposed but the bleeding stopped suddenly and the coagulation time returned to normal without lysis of the clot. Shock disappeared gradually after administration of 1,000 c.c. of blood under pressure. From then on the condition of the patient improved and the convalescence was normal. Laboratory tests showed interesting results. As stated, *in vitro* a micro-clot formed rapidly but dissolved immediately. The blood remained incoagulable for 24 hours. The Quick time was 37 seconds, corresponding to a prothrombin concentration of 5%. It should be noted that this clot also immediately dissolved in very fine fibrin shreds.

It had to be proved whether this phenomenon was due to lowering of prothrombin concentration (or its accelerators) or simply to a lengthening of the Quick time by hypofibrinogenæmia. To this effect we studied the influence on the patient's plasma of deprothrombinized and deproconvertinized normal plasma by adsorption on barium sulphate. The Quick time of adsorbed plasma was greater than two minutes. This plasma is commonly used as a diluent of normal plasma for the establishment of prothrombin curves. By diluting to 50% normal plasma having a Quick time of 13 seconds with an adsorbed plasma, we obtained a Quick time of 23 seconds. This prolongation was to be expected. The 50% dilution of patient's plasma with adsorbed plasma *also gave a Quick time of 23 seconds*. The patient's undiluted plasma had a Quick time of 37 seconds. If there had really been a prothrombin (or accelerator) deficit, the 50% dilution should have lengthened considerably the Quick time. On the contrary this was shortened to 23 seconds. This demonstrates that the prothrombin concentration of the plasma was normal. One may reasonably conclude that the adsorbed plasma has acted as a source of fibrinogen to shorten the Quick time. Looking at this problem from another angle, it may be said that the patient's plasma showed itself equal to normal plasma in its capacity to shorten to 23 seconds the nearly indefinite Quick time of deprothrombinized and deproconvertinized plasma. The patient's plasma collected before the end of the hæmorrhage had a small fibrinogen content as demonstrated by the thrombin time. Ten units of thrombin added to 0.1 ml. of plasma give, in the normal subject, a coagulum in three to four seconds. Our patient's plasma did not coagulate before 24 seconds. This indicates a low level of fibrinogen, not a complete disappearance. Such a finding would rather invalidate a diagnosis of absolute afibrinogenæmia but we have to take into account the significant quantity of whole blood and plasma (1,000 c.c. and 500 c.c. respectively) given by transfusion. Moreover, it is permissible to suppose that the disappearance of fibrinogen in a given individual may take

place more or less slowly and completely. Fibrinolytic enzyme may well digest the clots as they form without necessarily being able to destroy instantaneously all circulating fibrinogen. In our case the fibrinolysis was unquestionable; it happened under our eyes while we were studying coagulation by the test tube method. Moreover, we observed lysis of the clot obtained after recalcification of 0.2 ml. of plasma collected before the end of hæmorrhage. This was also observed for the Quick time clot. The control coagula were still very firm after 48 hours at 37° C.

DISCUSSION

The three cases reported have in common the following features: rapid and massive hæmorrhage, severe shock—which was in one case irreversible—and incoagulability of the shed blood. Our three patients had never had any previous hæmorrhagic accidents. The clinical course was not the same in all cases. Our first patient died in a few hours. Her blood was completely incoagulable. The second patient was in extremely severe shock but responded well to treatment. The disappearance of fibrinogen was not absolutely complete. A micro-coagulum formed, although it disappeared immediately. What is more interesting, the plasma of this patient did not coagulate after recalcification or addition of thrombin. Our third and last patient did not show a complete afibrinogenæmia. The collected samples coagulated, but with secondary lysis within a few minutes. Recalcification as well as addition of thrombin elicited a coagulum. This last case was fairly benign. Although the patient was in deep shock, the pulse was always perceptible and the blood pressure never went below 60/40 mm. Hg. Above all, the hæmorrhage ceased immediately after transfusion.

How can we explain these cases of defibrination? Excessive consumption of fibrinogen or destruction by fibrinolysis? These are the two principal hypotheses advanced to explain the phenomena. In the first theory[17, 18] defibrination is ascribed to the liberation of huge quantities of thromboplastin, originating in the operation wound or coming from an extensive raw surface such as that created in the uterus after separation of the placenta and membranes. This liberation of thromboplastin would reproduce what has been observed experimentally. When thromboplastin or thrombin is injected slowly into the blood stream of laboratory animals, the blood becomes incoagulable because of complete utilization of fibrinogen. This is defibrination by consumption. The other theory[6-9] ascribes defibrination to destruction of fibrinogen by a lysin. It is known that normal plasma contains a powerful antagonist to fibrinogen and fibrin. This substance exists in an inactive state (profibrinolysin, proplasmin, plasminogen), and is activated by an enzyme, fibrinolysokinase. Lungs and uterus are very rich in this activator of profibrinolysin. Liberation of fibrinolysokinase may be the cause of defibrination accidents. The fibrinolysin hypothesis seems to us the most convincing in our cases. The blood of our first patient never coagulated. As for the other two patients, there was an attempt at coagulation but the clot rapidly dissolved. The plasma of our second and third patients had a definite lytic action on control plasmas. It would be impossible to explain by any other theory the hæmorrhage in the third patient, who at the time had some fibrinogen left in her plasma. It seems logical to think that a lytic substance is responsible for the accidents. In some cases, e.g. Case 1, this substance was so abundant or active that it was able to destroy all fibrin as well as all available fibrinogen. In some other cases, this lysin is able to destroy the clot as fast as it is formed, without for this reason bringing about complete disappearance of all circulating fibrinogen. Uterine origin of this fibrinolysis was probable in our two obstetrical cases, but it is more difficult to determine the site of origin of the extremely potent lysin in our first case. We believe that this is the first report of defibrination following intestinal resection. The same accident may happen in thyroid surgery.[19] The aforementioned theories do not explain all cases of hæmorrhage by defibrination. It is not possible to discard as precipitating factors the shock which is always present, and effects of anæsthetics and curare-like substances. It must be admitted that, up to now, many cases remain unexplainable.

SUMMARY

Three cases of coagulation defect due to acute defibrination are reported. The evolution of these three cases was extremely serious. The first patient, a young boy of 14, died from shock and hæmorrhage following bowel resection. The second patient, a woman of 36, with hæmorrhage after a normal delivery, was saved by hysterectomy. We have demonstrated that excess of

fibrinolysis was responsible in this particular case. In the third case progress was identical, save that the episode ceased sharply after transfusion. Explanations of pathogenesis are discussed. The authors favour the lysis theory. The two surviving patients resumed normal hæmostasis a few hours after the episodes and this has been maintained ever since.

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RESORPTION ATELECTASIS WITH HYALINE-LIKE MEMBRANE*

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THE EFFECTIVE REDUCTION of neonatal mortality requires concentration of the greatest efforts on the first day of life when the majority of these deaths occur. Moreover, according to Bundesen and his colleagues,[3] abnormal pulmonary ventilation is the leading cause of death (43.7%), most of the latter occurring within the first 24 hours after birth.

Resorption atelectasis with hyaline-like membrane thus becomes a subject of great interest because, if this lung condition is proved responsible for the death of infants presenting these pathological findings, it coincides in time with the most frequent fatal disease in liveborn infants. We feel that such proofs are today fairly conclusive.[5]

Ahlström,[1] in 1937, was the first to suggest that this hyaline-like membrane might be the primary cause of death in some newborn infants. More recently, Potter[25] has stated that it was present as the only pathological abnormality in 40% of all infants weighing between 1,000 and 2,500 g. who died between 1939 and 1949 in the Chicago Lying-in Hospital. The exact incidence of this disease entity varies with the age groups and the authors from a low of 2.5%[17] to a high of 50%.[2, 20] There is no doubt that many infants must survive. Unfortunately, it is impossible to arrive at a specific diagnosis with the methods now at our disposal. We must rely entirely upon the clinical course for a diagnosis during life. However, the manifestations and evolution of this pathological entity are sufficiently characteristic to warrant accurate diagnosis in most instances.

Usually, the infant breathes spontaneously at birth, and afterwards appears normal for the first hour or two. Then, cyanosis and dyspnœa develop progressively until breathing becomes extremely laboured. The sternum and lower ribs retract with each inspiration and the breath sounds become gradually less audible. Death usually occurs in eight to 30 hours as a result of exhaustion and inability to obtain oxygen to sustain life. This clinical course may be illustrated by the following case history.

On February 4, 1952, Mrs. L., after a normal pregnancy and labour, was delivered easily at home of a male infant weighing 6 pounds and 7 ounces (3 kg.). Following nasopharyngeal aspiration, the baby breathed spontaneously. Two hours later, however, the doctor was called back because the baby was showing progressive cyanosis and dyspnœa. The child was admitted immediately to the pædiatric department of the Verdun General Hospital.

Upon admission, physical examination revealed cyanosis and dyspnœa with marked retraction of the lower portion of the sternum. The breath sounds were diminished in intensity. The rectal temperature was

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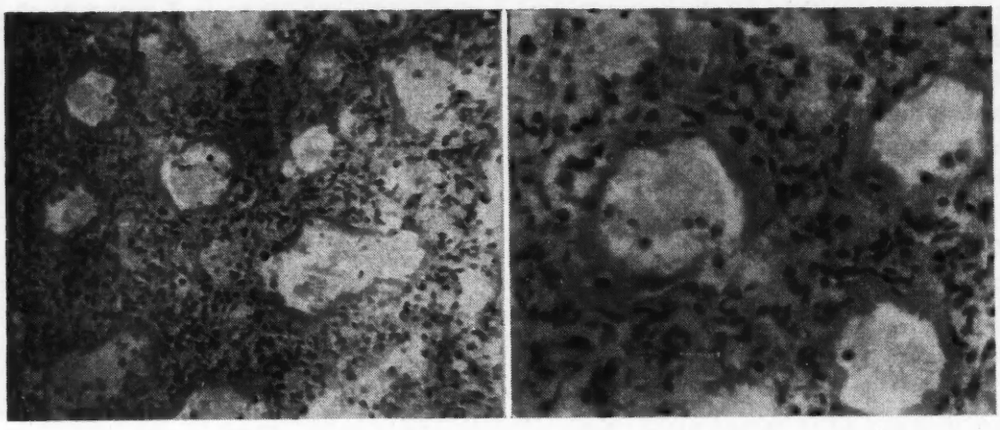

Fig. 1 Fig. 2

Fig. 1.—Photomicrograph of the lung showing hyaline membrane, resorption atelectasis and hyperæmia × 125). **Fig. 2.**—Photomicrograph of the lung showing hyaline membrane and resorption atelectasis (× 425).

94.4° F. It is of great interest to note that the mother had previously given birth twice to normal babies in normal circumstances, both dying with similar symptoms about ten hours later. To our knowledge, this is the first instance of a possible family trend.

A diagnosis was made of asphyxia by lack of oxygen reaching the blood through the alveoli, the clinical course suggesting the presence of a hyaline-like membrane. A chest film was interpreted by the radiologist as probably showing hypertrophy of the thymus. Special care must be taken in order to obtain an exact antero-posterior position, otherwise hypertrophy of the thymus may be incorrectly diagnosed at this age. Such was the case here.

The infant was placed in an incubator and given oxygen. Feeding was by gavage. The colour immediately improved but the respiration was still laboured. The following day, in spite of this treatment, the cyanosis had increased. Roentgen therapy of the thymus was attempted but death occurred at 4:30 p.m. on February 6, 53 hours after birth.

At autopsy, performed by Dr. Roger Beaulieu, the macroscopic and microscopic findings were similar to those of Potter.[26]

In general, when the lungs are opened, the lungs present a striking appearance. They are the size of well-expanded lungs but their consistency is that of liver. Instead of being yellow-pink as when containing air, or light violet as when not expanded (primary atelectasis), they are a uniform dark reddish purple. If the infant suffering from this disease survives more than 48 hours, an inflammatory process is usually superimposed. Then, on palpation, the lungs are slightly granular and ordinarily of uniform consistency. The whole lung or even slices sink in water despite the fact that a little air still remains in the proximal zones of the pulmonary tree. At this stage, the disease may be confused with pneumonia of the newborn.

Histological examination will reveal three types of lesion: (1) There is a widespread resorption of air and the walls of many alveolar ducts with most of the alveoli are collapsed, giving a solid appearance to the lung tissue between the few alveoli remaining open. This has been responsible for the name "resorption atelectasis" used by some authors. (2) Intense capillary engorgement produces the colour and increase in weight. This is one of the most striking findings on histological examination, classifying the condition as "congestive pulmonary failure" (see Fig. 1). (3) The inner surfaces of the alveolar ducts remaining open are covered by an irregular layer of homogeneous acidophilic material. In sections stained with hæmatoxylin-eosin, this substance has a hyaline-like appearance, with a darker pink coloration than either the red blood cells or the serum sometimes seen in conjunction with it. These staining properties justify the more popular denomination of "hyaline-like membrane disease" (see Fig. 2).

This disease forms a mechanical barrier to normal respiratory exchanges by blocking off some portions of the pulmonary tissue and by coating the remainder in such a way that the capillaries are deprived of their normal contact with atmospheric oxygen. Some polymorphonuclear leukocytes may be present, mostly in infants surviving more than 36 hours, but usually there is no evidence of infection.

The etiology and pathogenesis of this morbid entity have been studied extensively and several hypotheses suggested.

1. *Aspiration:*

Hoccheim[13] in 1903 was probably the first to find formations lining the walls of the alveoli in 2 of 43 cases studied. In his opinion, these formations were due to aspirated material "pressed by respiration against the alveolar walls and already undergoing changes under the influence of metabolism." Since the aspiration of amniotic

fluid is not a normal phenomenon, but occurs under conditions of asphyxia,[32] it is plausible to think that anoxia could be responsible for this condition. As a matter of fact, there is general agreement that suddenly induced anoxia, as in clamping the umbilical cord, frequently causes the fetus to make gasping efforts.[4, 28] Such strain may result in the entrance into the most distal portions of the lung of whatever fluid surrounds the baby. The term "vernix caseosa" was used first by Farber and Sweet[8] in 1931 to describe the appearance of the material found plastered against the walls of the alveoli and bronchioles of some newborn infants.

A second important factor would be age, since resorption atelectasis with hyaline-like membrane is never seen in stillborn infants or in those who die within one hour of birth or survive more than a week. It is also rare in babies weighing less than 1,000 g. and uncommon in those over 2,500 g. Thus it seems directly related to the stage of development at birth and the extrauterine age.[26]

2. *Infection:*

Steinharter[29] proved that these membranes are fat-free, possible evidence of aspiration by the fetus of amniotic fluid *in utero*. On the other hand, many authors suggest that this hyaline-like membrane may not be composed of aspirated vernix caseosa, meconium and amniotic fluid. Among others, Johnson[14] found bronchiolo-alveolar contents in the newborn, free of cornified epithelial cells. Miller and his coworkers[20, 21] demonstrated that the distribution of cornified epithelial cells did not correspond with that of the membranes. Also, they failed to produce a hyaline-like membrane by intratracheal introduction of vernix caseosa, meconium and amniotic content. Farber and Wilson[9] came to the conclusion that this membrane in the newborn is identical, in appearance and staining properties, with the hyaline-like membrane discovered in lungs of patients dying from the pandemic of influenza at the end of the first World War and from acute pneumonia of other etiology.[33] Only the pathogenesis would be different.

This membrane formation in the infant is often described in the pædiatric literature under the title of "pneumonia of the newborn."[14, 17] Thus, Johnson[14] in 1923 reported four cases of pneumonia in the newborn with the clinical course now regarded as characteristic of hyaline-like membrane disease. At autopsy, he found a hyaline-like membrane similar to that described by Goodpasture[11] in 1919 in cases of pandemic influenzal pneumonitis. However, there was no evidence of influenza in the mother, the family or the hospital staff, and moreover there was very little necrosis of the epithelial lining in the respiratory tree.

The resemblance to rheumatic pneumonitis was first noted by Masson[18] and later by Seldin[27] and Levy.[16] It was also described by Potter[25] in a four-month-old infant who died of chickenpox. The similarity of this membrane to that found in older persons dying of influenza or rheumatic pneumonitis suggests that an intrauterine inflammatory reaction might be a factor.

3. *Irritation:*

In radiation pneumonitis, a hyaline-like membrane has been described by Warren.[30] It has also been produced experimentally in dogs by the inhalation of cadmium chloride.[12] During their work to determine the pathogenesis of oxygen intoxication, Kuhn and Pichotka[15] produced hyaline-like membranes by subjecting animals to high concentration of oxygen at normal or elevated atmospheric pressure. Thus, oxygen intoxication is paradoxically a phenomenon of anoxia caused by this membrane. On the other hand, when oxygen is given to any infant beginning to show evidence of respiratory distress, Potter[25] feels that an increase in humidity to 90-95 degrees reduces the incidence of hyaline-like membrane disease.

Fauré-Frémiet[10] in 1920 showed that in the development of lung epithelium in the sheep a change occurs just before birth. While the connective tissue forming the parenchyma of the lung continues to increase, the epithelium lags behind and does not sufficiently cover the alveolar walls. Thus, we have in the fetal and neonatal lung a network without a continuous epithelial lining. This same discrepancy was described in the newborn by Potter and Loosli.[25] These observations seem to discredit the irritation theory of the epithelium.

4. *Innervation:*

Mendelsohn[19] in 1845 was the first to apply experimental methods to the production of atelectasis. Thus, he showed that section of the vagus was followed by atelectatic changes. A few years later, in 1851, Weber[31] confirmed that the cause of atelectasis lay mainly in the central nervous system.

Miller and his coworkers[22-24] produced a syndrome of resorption atelectasis in vagotomized rabbits and suggested that hyaline-like membrane formation in newborn infants may be related to the impairment or absence of certain central nervous system mechanisms, possibly vagal in location. Both these types of membrane contain a similar polysaccharide aldehyde.[22] Another proof of the importance of this neurological factor is the fact that in many infants dying of pulmonary complications after Cæsarean section there is an increase in subarachnoid fluid and it is known that pulmonary œdema can be produced experimentally by increased intracranial pressure.[6]

5. *Deficiency:*

Recent reports suggesting that premature births may be related to protein deficiencies in the maternal diet raise the question whether this pulmonary lesion might not be a deficiency disease.[7]

DISCUSSION AND CONCLUSION

From the preceding, it may be surmised that we are dealing with a very real and serious disease entity, responsible for a great number of infant deaths. The evolution of the pathological lesions may be divided into two phases: intra-alveolar transudation followed by formation of a hyaline-like membrane. We have reviewed the various factors capable of producing this transudate. We have also demonstrated that respiration is essential to the formation of this membrane. It is highly probable that contact of the transudate with dry, inspired air or oxygen determines the transformation of this transudate into the hyaline-like material.

During the first stage, it often should be possible to prevent the appearance of the second phase by placing the newborn infant in very humid atmospheric surroundings and by administering oxygen with great caution as to quantity and humidity.

When the second phase is already established, survival is still possible if the number of clear alveoli is sufficient to allow adequate respiratory exchanges, provided the procedures outlined for the first stage are used. Thus, if life can be sus-

tained long enough to allow lysis of this membrane by the leukocytes, the prognosis should become more encouraging.

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Case Reports

POSTOPERATIVE TETANUS

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POSTOPERATIVE TETANUS is an uncommon complication of elective surgery, but is such a serious one that every effort must be made to prevent it or to recognize it early, if it should occur.

In the cases reported[1, 9, 10] it has followed gynæcological operations most frequently and abdominal surgery to a slightly lesser degree, but it may follow any type of elective procedure. Most cases have been attributed to the use of improperly sterilized equipment or dressings, but catgut does not seem to be the cause it was once thought to be.[1, 4, 7]

The case reported here followed the second stage of a cross-leg pedicle graft. The operation was performed in a modern operating room, and all dressings and instruments had been autoclaved with the standard sterilization indicators in every pack. It was the only case of postoperative tetanus to have occurred in that institution.

Mr. B., age 30, was admitted on January 26, 1954, for treatment of an area of chronic ulceration on the lateral aspect of the right ankle and dorsum of the foot. The lower end of the leg and ankle had been run over by a car when the patient was four years of age, resulting in a compound fracture and subsequent osteomyelitis. The infection gradually subsided without the aid of surgery, but the patient was left with ankylosis of the ankle joint, interference with the epiphysis which resulted in retarded growth of that leg, and a chronic ulcer.

The patient was a well-developed man whose only abnormal physical finding was a chronic ulcer over the right lateral malleolus and dorsum of the foot, with extensive deep scarring surrounding it. There was 1½ inches (3.75 cm.) of shortening of the right leg.

On January 29, 1954, the patient was taken to the operating room and under sterile precautions the ulcer and the thick scar on the side of the foot were completely excised down to a more normal healthy bed. A pedicle was raised from the left calf and applied to the defect. The raw surface on the calf was covered with a split thickness graft removed from the back. The operative area was carefully dressed with absorbent cotton soaked in liquid paraffin, and flannel bandage. Plaster of paris was used to maintain the legs in their respective positions. He received 400,000 units of penicillin daily as a prophylactic measure for five days postoperatively.

On February 17, 1954, he was again taken to the operating room, where the plaster and dressing were completely removed. The pedicle had healed satisfactorily in the bed on the right foot, and the split thickness graft on the left calf had taken 100%. At this

stage the pedicle was divided and its base was set into the dorsum of the right foot after the thick scar had been removed in this area. The wound on the left calf was closed with interrupted black silk sutures. Both operative areas were covered with padded pressure dressings of absorbent cotton soaked in liquid paraffin, and flannel bandage. The patient again received 400,000 units of penicillin daily from February 16 to 20, and since he appeared well was discharged on February 22 with the sutures still present.

On February 23, the sixth day following the second stage of his graft, the patient developed general malaise, and complained to his wife of some stiffness in his shoulders and the upper part of his back. He also complained of some pain and stiffness in his right leg, but had done so from the time of removal of his cast. Later in the day he complained of a peculiar sensation in his jaw when he chewed.

On February 24, the discomfort in his jaw and the pain in his shoulders and back became more distressing. He was seen by his family doctor at that time, and reassured.

On February 25, he began having some difficulty in swallowing and complained of difficulty in getting his breath, and his jaw became increasingly stiff. He was seen on two occasions this day by his family doctor. His condition suddenly worsened on the evening of the same day; painful spasms began in his limbs and back, and stiffness in his limbs, neck and jaw became alarming. He was then brought to the hospital by ambulance.

A diagnosis of tetanus was made, and he was treated with 100,000 units of antitetanus serum intravenously, and 40,000 units subcutaneously around both legs above the sites of previous surgery. The operative area on the left leg and the donor area on the back were well healed, but there was a localized collection of serosanguinous fluid under the grafted area on the right leg, with very little surrounding inflammatory reaction present. The affected area was drained under local anæsthesia, the fluid sent for culture, and a drain left *in situ*. Aureomycin was begun intravenously, and intravenous Sodium Amytal and intramuscular phenobarbital were administered.

The patient was transferred to a quiet darkened room where nutrition was maintained with intravenous fluids, and sedation administered in the form of intramuscular Amytal and paraldehyde per rectum. The antibiotic was altered to penicillin in large doses, and a daily dose of 40,000 units of antitetanus serum was initiated. The patient's symptoms were only partially controlled on this regimen, and he continued to have tonic spasms intermittently. He ran a fever of up to 104° F. per rectum.

On February 26 he was clinically much improved, and was able to swallow but was still troubled by severe spasms. In the evening he suffered an attack of laryngeal spasm with apnœa and cyanosis, and an emergency tracheotomy was performed at the bedside.

The following day, February 27, his condition had begun to deteriorate, the spasms recurring frequently and severely, and the fever continuing unabated.

On February 28 the patient was no better; he was sedated to the point of unconsciousness without adequate control of the severe spasms, and periods of Cheyne-Stokes respirations began. Intravenous cortisone was begun on this day.[5]

On March 1 he was considered to be improved, but his temperature had been rising steadily, and early on the morning of March 2 he expired, his temperature being 107° F. per rectum just before death.

BACTERIOLOGY

A heavy growth of *Cl. tetani* was obtained from the serosanguinous fluid in the area on the right ankle. A complete bacteriological survey was made of the materials in the operating room which had been used in the skin graft operations, but no *Cl. tetani* was found.

DISCUSSION

We think that the infection probably began at the time of the second operation, as the more severe forms of tetanus have a shorter incubation period, and this seemed to be a severe form. The source of infection could not be determined, but certain facts would indicate that it was not introduced in the operating room. The bacteriological studies made on the materials used in the operation, the rigid sterilization measures and modern autoclaving equipment, and the fact that postoperative tetanus has not been seen in the hospital before or since, all would suggest that this was not likely a hospital infection.

The interesting possibility arises that this patient had tetanus spores lying in the thick scar about his ankle, having been introduced at the time of his original street accident 26 years previously; it was not until this scar was excised and the skin flap laid down at the second stage (producing anaerobic conditions) that the organisms were able to multiply and produce the disease. There is no way of proving or disproving this, and, although it seems incredible, it must remain a distinct possibility.

Another possible source of infection could have been spores present in the chronic ulcer of the leg, which undoubtedly had been contaminated frequently before his admission to hospital. This ulcer had been excised, however, at the first stage of the operation, twenty-five days before the onset of symptoms—an unusually long incubation period for symptoms of such severity. The clinical features and treatment of tetanus are well documented elsewhere,[2, 6] but one phase of treatment in this case requiring comment is the treatment of the site of infection. In this case the area was incised and drained. Present opinion in the literature favours excision of the site of infection,[6] and this might have been preferable to the method used, but the desperate condition of the patient at the time of admission influenced the choice of local treatment.

It is also worth noting that the period of apnœa and cyanosis requiring a tracheotomy seemed to mark a turning point in the course of his illness, his condition deteriorating from that time onward. An early elective tracheotomy

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might have changed the outcome, and such a procedure seems advisable in severe cases of tetanus in order to avoid the combined hazards of a period of anoxia and a hurried bedside tracheotomy.

An experience with a case such as this would make one think that active or passive tetanus immunization should precede elective surgery on old contaminated wounds. If the patient has been recently a member of the armed forces a booster dose of toxoid a few days before operation would suffice, otherwise 1,500 to 3,000 units of antitetanus serum should be given.[8]

SUMMARY

A case of postoperative tetanus following a cross-leg pedicle graft is reported.

A suggestion is made that all patients who are to undergo operations on old contaminated wounds or chronic ulcers should be protected by active or passive tetanus immunization.

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INFECTION WITH PASTEURELLA MULTOCIDA*

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THIS PAPER will present clinical, bacteriological and serological data derived from a case of gross sepsis of hand and arm. The patient was an Indian trapper, and the infection developed consequent to a laceration of the hand which he suffered while working on his trapline. The authors believe that *Pasteurella multocida* was a pathogenic agent involved in the production of the severe lesions.

Perhaps the most important purpose served by recording such a case is to draw attention to the occupation of the patient, which required frequent contact with animals. While there is not a copious literature on *Pasteurella multocida* infections in man, there is nevertheless an increasing awareness of the possibility that they may occur when external injuries are sustained in contiguity with an animal.

The patient was a 50-year-old male Indian trapper. He was brought in to hospital by plane from his trapline because of a greatly swollen and painful right hand and arm. His story was that he had cut his little finger with his skinning knife about a month previously. He was far from medical help and the finger became progressively more painful and swollen, until finally the entire hand and forearm were involved.

On admission he was extremely weak and his temperature was 102° F. There was extreme tense swelling of the right hand, both palmar and dorsal. The fingers were semi-flexed, swollen, and immobile, while over the palmar aspect of the proximal phalanx of the fifth finger was a deep cut from which some pus oozed. In the depth of this cut there appeared to be a necrotic tendon. Above the wrist the swelling was greatest over the pronator space. There was redness and induration extending to an inch or so above the elbow.

Multiple incisions were made for drainage of the palmar spaces, tendon sheaths and forearm space. Penicillin therapy was started at once. A culture of the pus obtained grew hæmolytic streptococci. Routine laboratory work showed a polymorphonuclear leukocytosis of 13,500 and a sedimentation rate of 117 mm. in one hour. Agglutination of *Pasteurella tularense* by the patient's serum was positive in a 1 in 50 titre. This subsequently rose to 1 in 100, where it remained on repeat readings throughout.

During the next two weeks his general condition improved greatly, and the swelling of hand and arm diminished to about half its previous extent. Purulent drainage continued, however, and it was decided to discontinue the penicillin and institute erythromycin therapy. After another three weeks there remained some slight drainage from the original cut and slight swelling of palm and lower forearm. A small tendon slough was being discharged through the cut. By April 3 drainage had ceased and the sinuses closed. Therapy was stopped, and within three days the hand became painful again.

On April 9 there was swelling and tenderness of the palm and forearm. Incision and drainage was again carried out and pus was evacuated from a deep isolated pocket overlying the pronator quadratus muscle. Cultures of this material grew a hæmolytic staphylococcus and a Gram-negative organism which was later considered to be *Pasteurella multocida.*

Aureomycin therapy was begun, and, somewhat empirically, streptomycin was also added. There was a dramatic response and by the end of three weeks no swelling was evident, the limb was painless and all incisions were soundly healed. Physiotherapy was begun and the patient soon returned to his home to await later reassessment.

The patient was seen again in January 1955. There had been no recurrence of pain, redness or tenderness. He had been using the hand actively in his occupation of trapping.

At this time the little finger was partly extended and no flexor power existed. There was power of flexion of the remaining fingers but inability to extend fully. Deep adhesions existed in the palm as manifested by lack of individual finger action and binding of the palmar fascia to underlying tendon movement.

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BACTERIOLOGICAL AND SEROLOGICAL FINDINGS

1. The first culture of pus on admission grew hæmolytic streptococci. 2. Following the relapse, pus was cultured on blood agar. After 24 hours at 37° C. a strong sperm-like odour was noted on opening the Petri dish. Besides hæmolytic colonies many non-hæmolytic colonies were found. The hæmolytic colonies were identified as *Micrococcus hæmolyticus* var. *aureus*. Microscopically, smears of the non-hæmolytic colonies showed Gram-negative ovoid-coccoid rods. A tryptose agar plate was inoculated with these organisms. After 24 hours at 37° C., translucent, greenish, smooth colonies were seen; after two to four days' growth a greenish edge formed around the colonies. Smears at times showed a tendency to bipolar staining.

Agglutination of suspensions of this organism with an immune serum (Lederle) containing antibodies to *Pasteurella multocida*, serological types I, II and III, gave the following results:

REMARKS

Because of the finding of the streptococcus initially and the staphylococcus later, it cannot be said that the infectious process in this case was all, or in part, due to *Pasteurella multocida*. However, the persistence of this organism in a deep pocket of pus weeks after penicillin and erythromycin therapy is interesting when one considers that such septic infections involving *Pasteurella multocida* have been reported by others. It would seem advisable to have this organism in mind when culturing pus from infections occurring in those who work in close contact with animals.

The presence of specific agglutinating antibodies to *Pasteurella multocida*, Type A, in the patient's serum one year later is interesting and the authors propose to investigate further the significance of such titres in Indians.

Serum dilution	*1:10*	*1:20*	*1:40*	*1:80*	*1:160*
Degree of agglutination.....	++++	++++	++++	++++	+++

AGGLUTINATIONS ONE YEAR LATER

Cultures of *Pasteurella multocida* of serological types A, B and C (I, II and III) were obtained from the Animal Diseases Research Institute of the Federal Department of Agriculture in Hull, P.Q. From these cultures suspensions of killed organisms were made for each of the three serological types for use as antigen. Agglutination of types A and C with the patient's serum, taken on January 18, 1955, one year after the original illness, gave the following results (all controls and all dilutions against type B were negative):

SUMMARY

1. A case of hand and arm sepsis is described, from which *Pasteurella multocida* was cultured.

2. The infection dated from a finger accidentally cut by a skinning knife.

3. The organism survived penicillin and erythromycin therapy but was controlled by aureomycin and streptomycin given together.

4. One year later the patient's serum showed antibodies to *Pasteurella multocida*, Type A, and to a slighter degree to *Pasteurella multocida*, Type C.

PASTEURELLA MULTOCIDA TYPE A AND PATIENT'S SERUM (JAN. 1955)

Serum dilution	*1:10*	*1:20*	*1:40*	*1:160*	*1:320*	*1:640 and higher*
Degree of agglutination.....	++++	++++	++++	++++	+++	Negative

PASTEURELLA MULTOCIDA TYPE C AND PATIENT'S SERUM (JAN. 1955)

Serum dilution	*1:10*	*1:20*	*1:40*	*1:80*	*1:160 and higher*
Degree of agglutination.....	++++	++++	++++	+++	Negative

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TRAUMATIC CHYLOTHORAX

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INJURIES suffered as a result of automobile accidents account for a large percentage of surgical cases in general practice, and the variety of the lesions encountered seems to be unlimited. Recently, the writer had occasion to treat a patient with chylothorax caused by such an accident; the case is being reported with the thought that these remarks may be helpful to others dealing with this condition.

The patient, a youth of 19, was first seen on October 15, 1954, because he could not get his breath properly and because he had developed a hacking cough when he smoked.

He stated that he had wrecked his car nine days before; and while the car was a total loss he didn't think he had been hurt badly. He was unable to work for a few days because of a pain in his lumbar region but this had responded to rest and heat applied locally. About a week after the accident he began to notice that walking around the house and climbing stairs made him breathe quickly and heavily and that smoking made him cough. There was no pain or sputum.

Except for a little pallor he appeared to be in good health, although even at rest he was breathing faster than normal. His temperature, pulse and respiratory rates were recorded as 101.6° F., 90 and 24 respectively. Positive physical findings were confined to the chest. A definite lag was noted in the right hemithorax on forced respiration. He indicated an area of tenderness over the right 9th rib in the anterior axillary line. The entire right thorax was dull to percussion and no breath sounds could be heard on that side. Examination of the left chest revealed nothing abnormal. The trachea was in the midline.

The impression at that time was that he had suffered a fractured rib with a resultant hydrothorax (or hæmothorax) which had become infected.

On October 16, a thoracentesis was performed under local anæsthesia and 1,850 c.c. of white fluid was removed. One million units of aqueous penicillin were instilled into the pleural cavity before the aspirating needle was removed. The fluid had the gross appearance of very rich whole homogenized milk, being a little more buff-coloured than the usual dairy product. Its specific gravity was 1.012. A few c.c. were added to an equal amount of ether, in which the fluid almost completely dissolved, leaving only a slightly turbid yellow fluid. No layering was noted in a sample of the fluid when it was left standing or after centrifuging. A specimen was forwarded to the Provincial Laboratory for identification of any organism present and determination of its antibiotic sensitivity. A second specimen was forwarded to Dr. John Patton at the Ottawa Civic Hospital, who confirmed the writer's suspicion that it was chyle.

On October 17 and 18, 850 c.c. and 550 c.c. of the buff-coloured fluid were removed. The patient was discharged to his home on October 18 with the advice to stay in bed and to follow a fat-free diet as he had been doing in the hospital. He returned to hospital as an outpatient on October 23, and 1,050 c.c. fluid was removed. The change in the fluid from a buff colour to an absolute white was remarkable. Because of a domestic problem which made it difficult for him to remain in bed at home, the patient was readmitted on October 26.

A series of aspirations on October 26, 28, and 30, resulted in 1,800, 1,500, and 1,000 c.c. of fluid being removed. On November 2, another "tapping" disclosed a second change in the fluid inasmuch as the 1,070 c.c. removed was a turbid yellowish watery fluid. On November 5, 700 c.c. of the same type of fluid was removed. No further aspirations were done, since on November 12 a chest film showed a minimal amount of fluid to be present. This film also revealed that a pneumothorax, noted at fluoroscopy after the thoracentesis on October 30, had almost completely resolved. It had accounted for about a 30% collapse when first noted. Also, this film, which was the best one taken up to that time, disclosed no fractured ribs. Fluoroscopy on November 30 showed a normal chest.

At no time during this illness, after the initial tap on October 16 relieved his respiratory symptoms, did the patient feel ill. The only suggestion of sickness was the fact that he lost about 10 pounds in weight, which he regained quickly. Aside from bed rest and the aspirations, the sole therapeutic procedure was to give a high protein and low fat diet.

DISCUSSION

According to Meade,[4] approximately one-half of all cases of chylothorax are due to direct or indirect injury, including injury during intrathoracic operations. Even trivial injuries[1, 3, 4] which may cause no other damage have caused chylothorax. In an appendix to his article, Meade refers to a 35-year-old woman who developed the condition after back-diving, an unusual form of exercise for her.

Relief of pulmonary compression is the most urgent consideration in order to regain lung function. If the condition is unrecognized, death from asphyxia may follow. A delay in treatment results in an intense fibrinous reaction of the pleura which prevents re-expansion of the lung. Incidentally, Meade[4] points out that decortication in these cases is extremely difficult due to lack of "peel."

Chyle is bacteriostatic, so that superimposed infection is not likely to be a problem. In the above case, the instillation of penicillin was not only unnecessary but possibly dangerous in an era of penicillin reactions. However, the diagnosis of chylothorax was not entertained until some study of the fluid had been made following the first thoracentesis. The bacteriological report stated that no growth occurred from a culture of the specimen.

Death in most of these cases is due to starvation because of the progressive loss of large amounts of fat, protein and fluid. Obviously it is more logical to prevent this wastage than to concentrate one's efforts on replacement, so that measures to stop the leakage are of prime importance although a high protein and low fat diet, blood transfusions, amino-acids and electrolyte solutions intravenously, and parenteral fat soluble vitamins have a place in sup-

portive therapy. Attempts to auto-transfuse the fluid have been successful in some cases and fatal in others, suggesting that this technique needs further study.[2-4]

The management of traumatic chylothorax should begin with repeated aspirations, since one-half of the patients in recorded cases have recovered with this procedure alone.[2-4] If there is no decrease in the amounts aspirated within 10 days to two weeks, closed tube-drainage should be tried, using suction if necessary. Thoracotomy, with ligation of the thoracic duct, becomes mandatory if this second measure fails to stop the leakage of chyle and to bring about re-expansion of the lung.

SUMMARY

The successful conservative treatment of a patient with traumatic chylothorax has been outlined, and a brief review of the pertinent recent literature on the subject has been presented.

The writer would like to acknowledge his appreciation to Dr. J. C. Samis of Ottawa and Dr. Fred Kergin of Toronto for their help in the management of this case.

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POST-CHOLECYSTECTOMY OBSTRUCTIVE TYPE OF JAUNDICE DUE TO CHLORPROMAZINE

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CHLORPROMAZINE (Largactil) was introduced several years ago by French workers and appears to be an effective agent in the treatment of neuropsychiatric disorders; as a sedative and as an analgesic and anæsthetic potentiator; as an anti-emetic; and to depress respiratory tract reflexes such as hiccups.

The incidence of toxicity of this drug seems to be relatively low but jaundice appears to be a definite complication and has been reported before. Denker[1] is said to have seen no jaundice in 450 patients treated with chlorpromazine, while Azima and Ogle[1] reported that 5 patients out of 100 treated with this drug developed jaundice. At least one fatality has been recorded[2] in which chlorpromazine appears to be the causative agent. Van Ommen and Brown[3] described three patients who developed jaundice while taking this drug and their first case is somewhat similar to the one below in so far as the jaundice was believed to be secondary to extrahepatic obstruction, and the patient had a laparotomy for a non-existent carcinoma of the pancreas. The mechanism of the jaundice induced is not too well understood. Initially, at least, there appears to be little hepatocellular damage and there is, rather, blocking of the finer bile canaliculi. For practical purposes it seems to be capable of producing an obstructive type of jaundice difficult to differentiate from other forms of obstruction.

The amount of drug given appears to have little influence in determining the development of jaundice, which can occur with minimal dosage. The time of onset of the jaundice can be predicted more accurately, however, and it usually occurs about the third week after the initial dose. Once established, the jaundice may vary both in severity and duration. One reported patient was still yellow at the end of seven months, and it is quite possible that this and other cases will unfortunately culminate in a hepatic cirrhosis.

The following case is presented as a jaundice due to chlorpromazine, complicated by the fact that the patient had had a cholecystectomy three weeks previously.

C.P., a 34-year-old married housewife, the mother of four children, was admitted to the North Vancouver General Hospital on January 13, 1955, for a cholecystectomy.

She had had symptoms of gallbladder disease for about one year with x-ray evidence of cholelithiasis. There had been no previous serious illnesses or operations. On admission, the sedimentation rate, the white cell count, prothrombin time and bromsulphthalein tests were normal. On January 15, a cholecystectomy was performed with relative ease. A choledochotomy was not done as there had been no clinical evidence of common duct obstruction, and at operation the duct was normal in size and there were no palpable stones. The pathological diagnosis on the tissue removed was "chronic cholecystitis, cholesterolosis, and cholelithiasis."

Postoperative recovery was uncomplicated except for excessive apprehension with some nausea and vomiting. She had Levin tube suction for 48 hours, and at the end of this time was given Largactil 25 mg. q.i.d. for a

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total of 350 mg. with good subjective and objective results. No transfusions or blood substitutes were given during her hospital stay.

She was discharged on the twelfth postoperative day feeling well, and she continued to improve until February 3—seventeen days after operation, when she had a one-day episode of chills and fever. Several days later she noticed that her stools were lighter and the urine darker in colour than normal. By the 21st postoperative day there was clinical evidence of jaundice associated with a mild pruritus. Apart from this latter symptom, she felt well and had no pain, no nausea or vomiting and no malaise. At this time it was felt that the differential diagnosis lay between a common duct stone and infectious hepatitis.

The jaundice increased fairly rapidly, and on February 17 she was readmitted to hospital. Laboratory tests at this time indicated an obstructive type of jaundice with a total bilirubin of 10.5 mg. %, with 64% direct; urinalysis showed bile in the urine and urobilinogen present in a 1:4 dilution. The cephalin cholesterol flocculation test was plus 2; the thymol turbidity 5; the alkaline phosphatase 20 Bodansky units; and the total cholesterol 248 mg. with 67% cholesterol esters. The fæcal urobilinogen was 1.2 mg. or 4.8 Ehrlich units. The serum protein level was 5.4 g. with a normal A:G ratio. The sedimentation rate was 19; the white cell count and differential and platelet count were normal. The prothrombin time was 100% before daily intramuscular vitamin K was started.

On February 20, Cholografin radiography of the ducts was attempted, but the biliary system failed to visualize.

Since chlorpromazine had recently been reported as a causative factor in obstructive jaundice, this diagnosis was considered and Dr. F. W. Hurlburt of the medical staff was asked to see the patient in consultation. He agreed that it was an obstructive type of jaundice and that chlorpromazine toxicity was a possibility, but believed that the common duct should be explored.

By February 25 the bilirubin had risen to 15.2 mg. and the cholesterol to 330 mg. The following day the common duct was explored under spinal anæsthesia. When the duct was exposed it obviously was not dilated and on needle aspiration contained only about 0.5 c.c. of clear bile. An operative cholangiogram was taken before the duct was opened, using 10 c.c. of 35% Diodrast through a small bore needle. An x-ray picture taken approximately 10 seconds later gave excellent visualization of the biliary tract with considerable dye in the duodenum and no evidence of stone or stricture in either the common duct or hepatic ducts. As it was felt best at this stage to confirm further the patency of the major ducts, the common duct was opened and explored in both directions with a catheter and probes. No sign of stone could be found and the duct was drained with a T-tube.

She made a good recovery from the second operation, although both the bilirubin and alkaline phosphatase rose to an even higher level for a short time postoperatively. On March 2 the bilirubin was 20.3 mg. % and the alkaline phosphatase 40.1 Bodansky units. Successive tests after this showed that the bilirubin level was gradually falling, and on discharge the level was 13.1 mg. %. Bile drainage amounted to approximately 80 c.c. per day and on the 10th day the T-tube was removed.

A liver biopsy was taken at operation, and reported on as follows: "There is considerable bile pigmentation of the liver cells about the central veins but for the most part the cells are quite well preserved. There is no particular inflammatory reaction in the portal spaces. There is no evidence of fatty metamorphosis."

She was discharged on March 14, on a 3,000 calorie diet consisting of 100 g. of protein and 300 g. of carbohydrate with oral Methischol. When last seen, one month postoperatively, the patient had few complaints but still had clinical jaundice of about the same degree as when she was discharged (see Addendum).

SUMMARY

Chlorpromazine (Largactil) appears to be a useful drug, especially in reducing the reaction to pain and controlling emotional tension, nausea, and vomiting. If it is used judiciously and with the knowledge that it has the ability to produce an obstructive type of jaundice, one may occasionally be able to prevent some morbidity and an unnecessary operation, as illustrated in the above case report.

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ADDENDUM

Three months postoperatively the jaundice had cleared but a moderate generalized pruritus remained.

Clinical and Laboratory Notes

FAILURE IN TREATMENT OF MULTIPLE SCLEROSIS PATIENTS WITH ISONIAZID*

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HYDRAZIDE of isonicotinic acid or isoniazid is the most effective drug recently introduced for the chemotherapy of various forms of tuberculosis.[1, 3, 5] As is usually the case with any new drug which proves potent for a specific disorder, isoniazid has been tried in the treatment of a variety of diseases of diverse etiology. However, only a few other bacterial conditions were found to respond to it favourably.[4]

In 1954 Kurtzke and Berlin[2] reported their results in the treatment of 30 multiple sclerosis patients with isoniazid. Using their own classification scale, they estimated that 90% of these patients were improved as compared with 33% improved in their control series. They further stated that certain patients treated with isoniazid

*From the Neurological Services of Shaughnessy Veterans' Hospital and the Vancouver General Hospital, Vancouver, B.C.
This investigation was aided in part by Federal Health Grants of Canada and the Vancouver Chapter of the Multiple Sclerosis Society.

were better within a few days of therapy and became worse upon withdrawal of the drug, to improve again following its reinstitution. Naturally, their conclusions have stirred up many hopes among practising physicians and multiple sclerosis patients following inappropriate publicity in the lay press.

PRESENT STUDY

It became necessary to investigate the real value of isoniazid in the treatment of multiple sclerosis. For this purpose 26 patients afflicted with the disease were given daily doses of isoniazid ranging from 200 to 300 mg., depending on body weight. A grading system allowing quantitative expression of their disability was developed. Patients were examined and graded at the commencement of the treatment, two weeks later, and every four weeks subsequently. Eleven of them were in hospital for a period of four weeks or longer. In addition to periodic objective estimation of the neurological status by the same examiner, the opinions of the patients themselves and their families were also recorded.

Six of the 26 patients worked full-time and the state of their disease was considered to be mild; three worked part-time only and their condition was considered to be moderately advanced; eleven were able to attend to their daily functions but were not able to work, their condition being considered advanced; the remaining six patients required help in their daily functions and their condition was considered to be severe.

In view of the totally negative results of the treatment of these patients with isoniazid, only a brief summary of the data is given.

Fourteen patients received isoniazid for a period of six months; in the remaining 12 cases the medicine was discontinued earlier for various reasons. One of the 14 patients treated with isoniazid for six months developed an exacerbation while on this drug and was hospitalized. The usual routine of five days' bed rest and subsequent gradual mobilization was instituted while the isoniazid was continued. The first signs of improvement were noted on the twelfth day; within a further four weeks' period his condition returned to the state in which it was before the exacerbation. It is well known that such improvement is not unusual in patients receiving only symptomatic treatment or even no treatment at all. Five patients of this group reported improvement while on the medication; the family of three of them also thought for a time that the patients were better. However, on objective examination no difference could be detected. The latter five patients were put on a placebo* for a period of six weeks and they continued to feel subjectively improved. The state of the remaining eight patients of this group was unaltered subjectively and objectively throughout the period of six months' treatment.

In twelve patients the isoniazid was discontinued before the end of the six months' period for the following reasons: seven patients desired to stop the medication themselves, five of them because of no improvement after a trial of three to five months, one because of progressive tingling and numbness in his hands and feet, and one because of an increase of dizziness. This last patient also claimed an increase of his symptoms when put on the placebo. Of the remaining five patients, the isoniazid was stopped in two for technical reasons (they moved to other provinces) and in three for medical reasons. Of the latter three, two developed an exacerbation while on this medication and the third fell down on the sixth day after commencement of isoniazid and fractured his left femur, subsequently blaming the medicine, stating that it "made" him more ataxic. One of the two patients who had an exacerbation was not improved after six weeks and showed signs suggestive of peripheral neuropathy; the other developed emotional disturbance and excessive euphoria, which improved following discontinuation of the treatment.

CONCLUSIONS

The administration of isoniazid to 26 patients with multiple sclerosis in this series did not prove unequivocally beneficial to any of them. Three patients suffered an exacerbation while on this treatment. Subjectively only five patients considered themselves improved, although this could not be substantiated by objective findings; four others thought that they were worse, and the remaining 17 did not feel any different. Mild side-effects were noted in three patients: one became emotionally disturbed and excessively euphoric and two others had symptoms and signs suggestive of mild peripheral neuropathy.

Unquestionably, therapeutic trials with specific drugs in hopeless chronic diseases are warranted and the history of medicine reveals examples of success from such an empirical approach. It is most unfortunate that in the case of multiple sclerosis innumerable specific therapies tried in the past 60 years have proved with melancholy regularity to be of no avail.

*A considerable portion of isonicotinic acid hydrazide under the trade name of Rimifon and also placebos were kindly supplied by Hoffmann-LaRoche Inc.

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Editorials

THE PREVENTION OF RETROLENTAL FIBROPLASIA

Loss of sight from retrolental fibroplasia (RLF) represents blindness in its most tragic form. Unlike those blinded later in life, these children have never seen the world about them, and their physical, mental and emotional development must take place under this handicap.

It is fortunate that in the past year or two the cause and means of prevention of this commonest cause of blindness in children have been discovered and proven. It is now of extreme importance that newly acquired knowledge be disseminated as quickly as possible, so that unnecessary cases will not occur.

Most Canadian physicians are aware that retrolental fibroplasia is caused by an excessive administration of oxygen in the early days of a premature baby's life. But certain practical points in the prevention of the disease require emphasis. This is of particular importance in view of the fact that modern incubators with improved facilities for providing high oxygen concentrations are becoming available to more and more hospitals throughout the country. More widespread opportunities for producing the disease are therefore accompanying advances in our knowledge of how to prevent it.

Wherever the following principles have been followed, uniformly gratifying results have been observed, viz., a virtually complete elimination of the disease, with no increase in mortality or morbidity:

1. Every nursery with facilities for giving oxygen to premature babies *must have an oxygen analyser.* Oxygen should then be *ordered by concentration and not by litre-flow,* since there is no adequate correlation between the oxygen concentrations in the incubator and the flowmeter setting.

2. Oxygen should never be given to premature babies as a routine measure. Only those showing clinical indications should receive it, and then in the lowest concentrations and for the shortest periods of time consistent with their needs. The initial concentration *should never be higher than 40%,* and this should be reduced as quickly as possible. In many cases, lower concentrations are sufficient. Banister[1] has shown that concentrations as low as 22 to 26% are often effective, especially in babies requiring oxygen over a period of time.

3. Oxygen concentrations in the incubator should be *measured and charted at regular intervals,* not less than four times a day. (Each of these measurements can be taken in a matter of seconds.)

4. Readings taken within 30 minutes of changing the flow-rate or opening the incubator lid or sleeves may be inaccurate, because there will not have been time for the oxygen concentration to become stabilized. These should therefore be repeated after the half hour has passed.

5. The chief indication for oxygen therapy is cyanosis. Periodic or irregular respiration in the absence of cyanosis is no longer considered to be an indication for oxygen.

6. In some incubators, designed before the dangers of oxygen toxicity were known, there is an attachment for providing a supersaturated environment, which is dependent on an inflow of oxygen. If supersaturation is desired in cases not needing oxygen, a compressed air pump rather than the oxygen inflow mechanism should be used.

7. Since the oxygen needs of the baby vary during the day, the control of the oxygen must be under constant surveillance. The nursing staff should be given the necessary training and authority to reduce the oxygen when it becomes apparent that the baby can get along with less.

A survey of the incidence of RLF between 1951 and 1953 in 17 nurseries in the United Kingdom has just been published by the Medical Research Council.[2] Of 344 babies weighing 4 lb. and less at birth, none who had had no

oxygen developed retinopathy. With increasing length of oxygen treatment, a steeply rising incidence of the disease occurred. Nurseries in which little oxygen was given and which were free of progressive retinopathy did not experience survival rates inferior to nurseries using more oxygen. A controlled co-operative study in the United States[3] involving 18 hospitals and 391 infants weighing 3 lb. 5 oz. and less at birth, gave similar results.

It remains important to determine whether proper control of oxygen therapy will entirely eliminate or merely reduce the incidence of RLF. Lanman[4] decries the growing concept that when oxygen toxicity is eliminated, an irreducible minimum of RLF due to other at present unexplained causes will remain. It is "unwarranted and dangerous . . . offers an excuse for the occasional case of blindness that may occur in a unit which uses oxygen in a manner which they may regard as sparing." He believes that RLF appearing in an infant who has received any added oxygen must be attributed to oxygen toxicity until proven otherwise. Growing experiences at the Royal Victoria Hospital, Montreal,[1] support this belief and suggest that *complete* prevention through proper control of oxygen is an entirely plausible goal.

Public health authorities, hospital administrators, and those responsible for hospital accreditation should now give serious thought to their responsibilities in the prevention of this disease.

Public health authorities can issue directives to physicians and hospitals, as has been done with dramatic results in New York and Maryland. Because of frequent turnover of intern and nursing staffs, these directives should be prominently displayed in the nursery.

Hospital administrators can ensure that their nurseries are adequately equipped to provide the extraordinary care needed in the administration of oxygen to premature babies. They can see that orders for oxygen are written as specific concentrations, just as is done in the ordering of potentially toxic or lethal drugs, and that these concentrations are affirmed by the repeated use of an oxygen analyser.

Finally, those responsible for hospital accreditation can, in the light of recent experiences, underline the need for careful and controlled use of oxygen in the nursery, and use their influence to safeguard against impaired vision or blindness in our babies.

JOHN C. LOCKE

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ANTIMICROBIAL THERAPY OF TUBERCULOSIS

Ten years have now elapsed since the isolation of streptomycin and its application to the treatment of tuberculosis. During this period of time, there have been numerous changes in our concepts regarding the antimicrobial therapy of tuberculosis, not only with streptomycin but also with the newer agents which have since been discovered, particularly PAS and isoniazid. It now appears necessary to collect the available information, assess its value, discard what is valueless and provide an acceptable general background for the present-day antimicrobial management of all forms of tuberculosis. Apparently by coincidence, attempts along these lines have recently been made by both the American Trudeau Society Committee on Therapy and the Committee on Chemotherapy and Antibiotics of the American College of Chest Physicians. Although there are minor divergences in the recommendations of these two bodies, the major outlines are essentially similar. Both reports concede that the best available antimicrobial agents for the treatment of tuberculosis are streptomycin (or dihydrostreptomycin), PAS and isoniazid. It now seems clear that viomycin is too toxic for general use, and should be reserved for administration, with great care, to patients whose tubercle bacilli are resistant to one or more of the routine preparations. Iproniazid appears to have little to recommend it as compared with isoniazid, and is distinctly more toxic. As for pyrazinamide, its proven hepatotoxicity precludes its general usage and it should be reserved for careful administration only in very unusual circumstances. Oxytetracycline has not been routinely used in the treatment of tuberculosis, although it has been shown *in vitro* to have a restraining effect

on the emergence of streptomycin-resistant tubercle bacilli.

Given three potent antimicrobial agents, the question arises as to their mode of usage. It is clearly established in both of the reports that the individual use of these drugs should be frowned upon. That being the case, there are several possible combinations of these three preparations, all of which have had exhaustive trials. Until recently the most popular combination was streptomycin in an intermittent regimen (1.0 g. twice weekly) together with PAS (12.0 g. daily). This has, to a certain extent, given way to the combination of intermittent streptomycin together with isoniazid, the latter in a dosage of 5 mg. per kg. Another possible combination consists of PAS and isoniazid, both in a daily regimen and in the doses mentioned above. It would appear that this latter combination should be reserved for patients hypersensitive or intolerant to streptomycin (or dihydrostreptomycin), either initially or as a result of previous heavy dosage. Finally, the combination of all three antimicrobial agents has been used by some workers, and, although doubts have been cast on its special efficacy, there continues to be a natural tendency to use this combination in dangerously ill patients.

It must not be assumed that the administration of streptomycin is entirely confined to the intermittent type of regimen described above. In patients with miliary tuberculosis, tuberculous meningitis and far-advanced highly active pulmonary tuberculosis, the daily administration of streptomycin (or dihydrostreptomycin) for relatively short periods of time is sanctioned. It should also be made clear that, while in ordinary forms of tuberculosis treatment may be carried out without isoniazid, in miliary and meningeal tuberculosis the use of isoniazid is mandatory. One should also stress the point that in these latter forms of tuberculosis the dose of isoniazid is usually increased to 10 mg. per kg. A rather important discovery along these lines has been that isoniazid, if given in a dosage of 8 to 10 mg. per kg. in cases of primary or miliary tuberculosis, will prevent the development of tuberculous meningitis.

A word about drug toxicity appears indicated at this point. The toxic effects of streptomycin, dihydrostreptomycin, and PAS are well known and require no enlargement here. It is of some interest to note, however, that contrary to earlier opinion, isoniazid is not without its own toxic manifestations. Reports are now beginning to appear in the literature describing a peripheral neuritis syndrome, undoubtedly due to isoniazid when given in high and prolonged dosage. This toxic effect appears to be closely connected with pyridoxine metabolism, and reasonably satisfactory results have been obtained by discontinuing the drug and instituting pyridoxine therapy. It should not be forgotten that, entirely distinct from actual toxicity, all these antimicrobial preparations may induce hypersensitivity effects, even when given in small dosage early in treatment. It is of some importance, therefore, for chest physicians to be familiar with the various methods of desensitization, as well as the alternative antimicrobial agents that may be substituted for those to which a patient has exhibited hypersensitivity.

A feature common to all antimicrobial preparations in the treatment of tuberculosis is the development of bacterial resistance. In the early days of antimicrobial therapy for tuberculosis, particularly when only one of the agents was available, this feature assumed more importance than it does at present, and the various combined regimens described above have been devised with the specific purpose of preventing or delaying such bacterial resistance. Nevertheless, this situation still occasionally constitutes a problem, and the phthisiologist must at all times maintain a rather delicate balance in the interpretation of *in vitro* sensitivity tests as compared with the patient's clinical progress. It should be clearly understood that, with all these antimicrobial agents, the demonstration of bacterial resistance in the laboratory is not always clinically significant. This appears to be particularly the case with isoniazid, which, for some as yet unknown reason, seems to produce a permanent diminution in the virulence of tubercle bacilli, even when the laboratory findings appear to demonstrate a high degree of bacterial resistance to this agent.

While more thoughtful workers in the field of tuberculosis continually stress the admonition that the availability of potent antimicrobial agents should not result in the abandonment of sound surgical principles in treatment, there is no doubt that these preparations have materially altered our thinking in this connection. This is

particularly striking in the case of genito-urinary tuberculosis. It now seems clear that, in many cases, acceptable "cure" with more or less permanent sterilization of the urine may be obtained in tuberculosis of this system, as the result of intensive antimicrobial therapy, without recourse to surgery. In many cases, it has been found unnecessary to sacrifice an entire kidney when a residual localized abscess remains after such intensive medical treatment. Under present circumstances neither nephrectomy nor epididymectomy is an emergency procedure, and they can almost always wait for careful evaluation of the individual case following intensive medical treatment. If this plan is followed, it is frequently possible to "cure" a patient by segmental resection of a kidney, partial resection of an epididymis, or no operation at all. The trend is therefore more and more in the direction of conservatism in the management of genito-urinary tuberculosis, although the same cannot honestly be said in the case of pulmonary tuberculosis.

In spite of the prevalence of untutored over-optimism, particularly as evidenced in the lay press, much remains to be done and numerous changes remain to be made in the antimicrobial management of all forms of tuberculosis; one can foresee changes in concepts, adjustments in viewpoints and revolutions in management for some years to come. S.J.S.

Editorial Comments

POLIOMYELITIS AND TONSILLECTOMY

The latest in a series of investigations into the relationship between tonsillectomy and poliomyelitis has recently been reported (*Lancet*, 2: 5, 1955). It is a Medical Research Council Report of work done in England and Wales in 1951-53, and confirms to a large extent the findings of American and Australian observers. Two separate inquiries were made, into recent and remote tonsillectomy respectively.

In the first, 114 cases of poliomyelitis were collected in children under 18 who had undergone tonsillectomy during the three months preceding the onset of poliomyelitis. There were 34 spinal, 29 spinal and bulbar, 27 bulbar and 13 non-paralytic cases, with seven deaths. No less than 61 of the group developed poliomyelitis within 21 days of operation, and in these there was an unusual preponderance of bulbar cases. It is impossible to decide whether the spinal and non-paralytic cases were coincidental, and only some of the bulbar cases were due to operation, or whether all cases had some association with the tonsillectomy. The reporters consider that tonsillectomy adds only a few to the total number of cases, and therefore presents only a small problem to the community.

"As a problem for the individual whose tonsils are removed it is important. The practice of stopping tonsillectomy in the late summer and early autumn or when poliomyelitis is epidemic may diminish the number of postoperative cases; but even if tonsils were removed only in the first six months of the year, the risk of developing bulbar poliomyelitis soon after the operation would still be present. In addition there might be increased risk of other complications of tonsillectomy, such as intercurrent infection."

The second inquiry embraced two series of hospitalized children under 16, one series with poliomyelitis and the other with other conditions; in both series the presence of tonsillectomy at any time in the past was recorded. It appeared from statistical study that the removal of tonsils even five or more years previously made patients with poliomyelitis more liable to develop the bulbar or bulbo-spinal form than the spinal-paralytic form. In other words, removal of tonsils was responsible for the development of bulbar or bulbo-spinal poliomyelitis in some children who would not otherwise have had it.

Tonsillectomy therefore is a calculated risk; the slight chance that the candidate for tonsillectomy may later develop bulbar rather than spinal poliomyelitis has to be weighed against the greater chance of his continued ill health if the tonsils remain in.

ALLERGY AND RH FACTORS

"The frequency of allergic manifestations was investigated in 455 Rh-negative non-transfused women immunized against the D-factor by pregnancy and in a control material consisting of 461 Rh-negative non-transfused women with an Rh + (D +) husband, but not immunized, and with a number of pregnancies approximately equal to the number of pregnancies in the immunized women. The frequency of allergic manifestations in the relatives of the women of the two groups was also investigated. No statistically significant difference could be demonstrated between the frequency of asthma, hay fever, vasomotoric rhinitis, prurigo of Besnier, eczema, urticaria or œdema of Quincke in the two groups. It could not be demonstrated that the allergic women were immunized against the Rh (D) factor by fewer stimuli than the other women. No difference could be demonstrated in the titre of the Rh antibody made by the allergic and the non-allergic women."—Helge Heistö: *Acta, path. & microbiol. scandinav.*, 37: 63, 1955.

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PUBLIC RELATIONS FORUM

I. THE FIVE W'S OF MEDICAL PUBLIC RELATIONS

[We are happy to publish this article, the first of a series on public relations of the individual doctor, contributed by Mr. L. W. Holmes, the new Assistant Secretary of the Canadian Medical Association. Such articles are particularly valuable because the author, being a layman, is able to appreciate the points of view of both physician and patient.—ED.]

Public relations! Probably no other phrase has been more used and abused by industrial, business, professional and organizational people during the past two decades. Yet many have only a vague concept of the meaning and the methods of public relations. In a society as complex as ours, where so much depends on public relationships, sound knowledge of the fundamentals of public relations is necessary.

It is on that philosophy that this series of articles is based. It seeks to answer the five W's—*What? Why? Who? When?* and *Where?*—and the *How?* of public relations. This introductory article treats the five W's; subsequent articles will discuss some of the specifics of the "How" of public relations.

WHAT IS PUBLIC RELATIONS?

Public relations is a practice; it is a philosophy; and it is a state of interrelationships. It is both means and end. As a practice, public relations is a means involving techniques designed to inform and persuade within the dictates of a predetermined policy. The goal of public relations practice is good public relations—the end. This really means good public relationships—good will, if you wish. Underlying it all is the philosophy of public relations: that in this complex world the component parts of society must be brought into close harmony. This can only be achieved through known good works springing from good intentions.

What, then, is the meaning of this tripartite phrase? Combining the different aspects we have discussed, one could safely give this definition:

Good public relationships achieved through sincere good works and good, two-way communication.

WHY PUBLIC RELATIONS?

The easiest way to answer this question is to look at some of the obloquies evoked in a conversational sample of a small, but important fragment of public opinion:

"Those (so-and-so) doctors are just a bunch of money-grabbing, fee-splitting, high-and-mighty mechanics. . . ." "I've wasted a lot of valuable time cooling my heels in outer offices waiting for doctors. . . ." "They treat you more like a piece of machinery than like a human being. . . ." "You can't get them when you really need them. . . ."

And much more!

Of course some of these critics, particularly those who deal in the vague commodity called "public opinion," were aware that they spoke in generalizations. As one put it:

> "There are some fine doctors. My family physician is a good example. He's my idea of a good, honest, considerate Joe. Maybe he's not as up-to-date as some, doesn't have a lot of fancy equipment or a modern office. But he's interested in me and my family and he's done an excellent job of looking after us for a number of years."

That appears to be the state of affairs today. The non-medical individual is generally satisfied with his family physician, but highly critical of the amorphous mass he terms "the medical profession."

The remedy is a sound public relations programme, and I use the phrase "public relations" in its composite sense. Public relations will promote the harmonious public relationships which the medical profession must have if it is to remain free to choose its own way.

WHO IS RESPONSIBLE FOR PUBLIC RELATIONS?

Before we plunge into this part of our discussion, let's look at why our non-medical friend feels the way he does. A few observations on the nature of *public opinion* may shed some light on the subject.

Public opinion is but the concert of individual attitudes. And these individual attitudes spring from the myriad forces at work in one's environment—familial, institutional and personal.

James E. Bryan, author of "Public Relations in Medical Practice," which book, incidentally, I would recommend to the reading of every Canadian doctor, makes this observation:

"The public relations of American medicine is the sum total of the impressions that individual physicians register in the minds and hearts of their individual patients and friends."

(If one reads "Canadian" for "American" in that statement, the meaning is not changed.)

These postulates should answer why the non-medical person disapproves of "the medical profession." He is only voicing his reaction to personal unpleasant experiences with doctors, or stating an opinion influenced by others who have had such experiences.

It should be obvious, then, that our public relations programme must begin at the level where public opinion is shaped—at the level of the individual. This places the onus upon the individual doctor. It is in his daily contact with people, in the office, in the club, on the golf course, in church, wherever it may be, that he must launch his attack against poor public relationships.

WHEN, WHERE SHOULD PUBLIC RELATIONS BE PRACTISED AND SOUGHT?

The remaining two of our five W's of public relations have already been answered. Public relations is a continuing, day-to-day process, involving the doctor in all areas of activity; it is not something to switch on when office hours begin and off when the last patient leaves. It is, after all, an application of the greatest public relations guide given mankind:

". . . all things whatsoever ye would that men should do to you, do ye even so to them. . . ."

PUBLIC RELATIONS EXCHANGE

From time to time individual doctors and medical societies institute, knowingly or unknowingly, public relations practices which have won many friends for themselves and the profession as a whole.

These may include such activities as friendly monthly letters to patients, unusual reception room accessories, techniques to improve the services of office assistants, or methods of publicizing society activities.

Whatever the form these public relations techniques may take, why not share them with others? This may be done by sending an outline to Association offices, 244 St. George Street, Toronto, Ontario. Periodically they will be reported in these columns so that others may consider their adoption.

STATEMENT OF POLICY ON HEALTH INSURANCE

All too frequently the medical profession's stand on health insurance has been misunderstood and misrepresented. To correct this situation, the Association has prepared a four-page leaflet setting forth the "statement of policies and principles on health insurance in Canada" as adopted by General Council in June 1955. These reprints are being distributed to individuals and groups known to be interested in health insurance.

However, since it is difficult to obtain the names of all groups and individuals who might be interested in this subject, particularly at local and provincial levels, you can help.

If you know of persons and organizations who have taken or may take a stand on health insurance, please send the names and addresses of such parties to Association offices, 244 St. George Street, Toronto, Ontario, so that these statements may be sent to them. Or copies will be mailed to you, if you wish, for local and regional distribution.

Men and Books

OUR GOUTY PAST*

WALLACE GRAHAM, M.D. and
K. M. GRAHAM, B.A., *Toronto*

LIKE MIND AND BODY, history and disease are inseparable. There is historic interest in the autopsy on Napoleon which revealed an unsuspected carcinoma of the stomach, in the tragic insanity of George III, and the devastating gout of Pitt the Elder, but the fascination lies not in the morbid anatomy of the ailment and its effect upon an historic figure but in its effect on the history of mankind. If we dramatize the long history of man, disease has played a subtle but prominent role, a single actor bringing joy, gloom or despair, well recognized by the contemporary critic but largely neglected by the historian.

It was this fascinating reflection which led us to try to trace the history of gout from the earliest records to the present day. Gout is a rather obscure disease but it left its mark not only on the bodies of those afflicted but also on literature, art, drama, and government, even possibly turning the tide between war and peace throughout the centuries: a study of these aspects brought much new material to light.

The gouty, unlike those stricken by other unshakable maladies, seldom achieve a state of Christian resignation. Gout tends to inflame their tempers, and extreme cantankerousness has been considered a definite symptom of the disease.

Perhaps the most caustic of all attacks on the disease was written by Ellwanger, in 1897. Gout, he stated, is a "perverse, ungrateful, maleficent malady that delights upon the slightest pretext in assaulting vulnerable humanity at the most unseasonable hours and inconvenient times . . . a stealthy, rancorous, irascible, mordacious disorder—the wolf of diseases . . . its poison comes by heritage, its venom lurks in the wine cup, its seeds are sown at the gatherings of good cheer."

Ordinarily, the sight of a man suffering almost unendurable pain stirs his friends and loved ones to tender expressions of pity, but not so with gout. Almost all who are not afflicted seem comfortably persuaded that it is a laughing matter and that it has much in common with a hang-over. William Cowper (who did not have gout) shared this stern ungenerous view when he referred to the pain as "Pangs arthritic that infest the toe of libertine excess."

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*Read at the Toronto Academy of Medicine Library and Historical Night, March 1, 1955.

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The violent reaction of the many gouty people who are teetotallers and often vegetarians as well, but who find their disease constantly associated with wine, women and song, needs no further elucidation.

The specific treatment for acute gout contained in colchicum or the autumn crocus has now been recognized for over one hundred years. However, a study of ancient herbals and medical books reveals that hermodactyl or meadow saffron, now known to be identical with colchicum, was used at least fifteen hundred years ago. Why the specific cure was dropped from general use for hundreds of years is brought to light in the historical writings on this mysterious disease.

In the winter of 1872, the German Egyptologist, George Ebers, came into possession of the papyrus which bears his name. While excavating in the vicinity of Thebes, he was approached by an Egyptian who handed him a metal case, and inside wrapped in old mummy-clothes was a huge roll in a perfect state of preservation. It was 12 inches in width and 68 feet in length, and the date has been confirmed at 1500 B.C.

Among the many pathological conditions described in this papyrus, gout is not identified, but among the 811 prescriptions set forth are those containing the crocus—crocus from the south—crocus from the hills—crocus from the Delta—and saffron and saffron seeds, which perhaps suggest that the remedy for gout, colchicum, may have been known 3,500 years ago.

That the ancients were fully aware of the nature, symptoms and treatment of gout is at once evident from a perusal of their writings. It is true that the term gout was not introduced till the end of the 13th century. The Greek physicians called it podagra, and even in the second century we find a satire by the Greek poet Lucien, called the "Tragedy of the Gout." We will quote only a few lines in translation.

"But when the spring revives the blooming elm, and on the sprouting twigs the blackbird sings. Then shoots an unseen hand into our limbs, a fiery dart which like lightning, flies through all our veins and arteries and joints, gnaws, pierces, tears, devours, inflames and burns, till the great Goddess calls her torments off."

The writings of Hippocrates, who lived about 350 B.C., show that he was well acquainted with gout, and his aphorisms indicate a considerable knowledge of this disease. His prognosis would be largely admitted to the present day.

"Those who are old or who have chalk stones formed in their joints or lead a laborious course of life or have dried bellies cannot be cured by any human means. Young persons not having tophi formed in their joints and who live guardedly, and whose bowels will bear the proper treatment may be cured." He advocated the burning of flax on the affected joint and this strategy seems to have remained in vogue for nearly 800 years.

According to Galen gout and arthritic complaints are caused by an unnatural accumulation of some humour in the affected part. The humours were phlegm, bile, blood or a mixture of them or simply a crudity. This crude humour, he remarks, sometimes solidifies into tophi. The offending humour must be evacuated by bleeding or purging with the application of repellents and discutients.

Seneca mentions it as a monstrous example of the depravity of his age that the women by their luxurious habits had become subject to the gout. "The nature of women is not altered," he says, "but their manner of living, for while they rival the men in every kind of licentiousness, they equal them too in their very bodily disorders. Why need we then be surprised at seeing so many of the female sex afflicted with gout?"

Aretæus, in the 2nd century, also had a clear conception of gout: "The pain first seizes the great toe, then the forefront of the heel, the hollow of the foot and afterwards the ankle." He mentions the recurrent nature of the disease and recalls that a gouty patient had, during the interval of freedom from the disorder, even won his race in the Olympic games.

The works of Alexander of Tralles who wrote in the 6th century contain the first record of the use of colchicum in gout. Alexander begins by censuring the practitioners of his day, who said that gout was incurable by the art of medicine. This he states is not the case, but some do not choose to submit patiently to the methodical plan of treatment, but insist upon getting medicine to allay at once the violence of the pain. For this purpose, he says, hermodactyl (colchicum) is particularly trusted to by some and seldom fails to remove the pain. Unfortunately he had included hermodactyl simply as a purge, and before long substituted a less violent one, and the specific drug was thus lost to medicine for many years.

Also about 500 A.D. there lived a Mesopotamian physician called Aetius who seems to be a man of unlimited whimsicality. He recommended a month-by-month programme for sufferers from gout. In January, take a glass of pure wine every morning; in March, mix sweets with eatables and drinkables; in April, refrain from horse-radish; in July, abstain from venery, and so on.

Paul of Aegina (600 A.D.) was the last of the Greek eclectics and compilers. He notes that sorrow, care, watchfulness and other passions of the mind may also excite an attack of the disorder. He recognized the value of colchicum as good for affections of the joints and rheumatism and bad for the stomach, so that it should be used only by those pressed by urgent business. The violent effects of the purging caused by colchicum were apparently leading to a reaction against this valuable drug.

In 640 A.D. the great university and library at Alexandria were destroyed, and the means of preserving and spreading Greek doctrine to the East was lost. No other prominent medical authors are to be found in Christian Europe until the gloom of the Dark Ages begins to be dissipated in the 14th century. Not long after the extinction of Greek learning, another race

Fig. 1.—A Sudden Call, or one of the corporation summoned from his favourite amusement.

took the place of the Hellenes. The Arabs turned with marvellous quickness from piratical conquest to the higher pursuits of peace, and soon built up schools at Baghdad in the east and at Cordova in the west. Of the Arabian physicians, Serapion, Rhazes and Avicenna joined in praising the virtues of hermodactyl in gout.

We now enter the 15th century. The Dark Ages are over and the age of reform or of progressive medicine begins. The first two centuries of the renaissance of medicine were those of servility to the ancients, but for the first time universities and schools were increasing in number. At Paris there were in the 15th century about 25,000 students, and in England at the beginning of the 16th century Thomas Linacre founded the College of Physicians and Surgeons in London and established Chairs of Medicine at Oxford and Cambridge.

Henry VII came to the throne in 1485, and we read that in the two and twentieth year of his reign (1507) he began to be troubled with the gout. His marriage to Lady Margaret, Duchess of Burgundy, was postponed in respect of the infirmity of the King, "being troubled with gout and tissick."

In 1560, there was printed in England a Method of Physic, by Phillip Barrough, containing the causes, signs and cures of inward diseases in man's body from the head to the foot. The seventh edition, perhaps the earliest medical book in English in our library, contains a fascinating chapter entitled "Of the Gout in the Feet and Joints". It was dedicated to Lord Burghley, High Treasurer of England, in the time of Queen Elizabeth. In this book we read:

"Podagra and arthritis in Latin be diseases of one kind, and therefore they differ not but in places diseased, for in both of them there is weakness of the joints and an unnatural humour floweth to them, and if that the fluxe of the humour do flow to the feet, that is called podagra in Latin, but if the humour flow to the joints, it is called in Greek arthritis, in Latin articularis morbis, the joint sickness. Sometimes the evil doth rush in suddenly, being equally dispersed throughout all the joints, but for the most part the fluxe is wont to fall in privily, and by little and little. For in some pain doth invade the joint of the great toe. . . . This disease is engendered of continual crudities and drunkeness, and of immoderate using of lechery, through vehement and swift deambulations and walkings, by suppressions and stopping of accustomed excretions and fluxes and through intermission of familiar exercises. Perturbations of the mind do not only engender this evil, but also do breed hurtful and corrupt humours."

In the section of remedies of this same book are found prescriptions for pills containing colchicum—"which do draw out ferrous or waterish humours mightily from the furthest parts, especially from the joints" (1560).

In a German book called *Medizinisches aus der Geschichte* (Diseases of the Famous), we find some interesting facts about the clergy. Hertzog Christian von Wurthenburg wrote a long treatise on gout in 1537. At this time he was suffering from severe gout himself, and he gave instructions to Martin Luther about how to treat his gout. The same book describes the many diseases of John Calvin, who besides gout had malaria, stomach trouble, migraine, insomnia, hæmoptysis, lung infections, hæmorrhoids, renal colic and stone. When we add to the names of Luther and Calvin that of John Wesley, afflicted with gout in the 18th century, one wonders how the Presbyterian, John Knox, escaped.

With the 17th century we enter a period of scientific research, and servility to ancient authority ceases. Francis Bacon, who also had gout, founded inductive philosophy, and Descartes elucidated the principles of scientific method, all of which tended to emancipate the human mind.

William Harvey, who applied these methods to discover the circulation of the blood, was known to be "much and often troubled with the gout, and his way of cure was thus: he would sit with his legs bare if it were frost on the leads of Cockaine House, put them into a pail of water, till he was almost dead with cold, then betake himself to his stove, and so 'twas gone," an interesting example of what we now call contrast baths.

As well as establishing Boyle's law and inventing the air pump, Sir Robert Boyle (1627-91) seems to have taken an interest in gout, and mentions the cure of gout by fright. "A gouty

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man with hands and feet covered with poultices of turnips, flour and milk, was left in his chair in a low room while the servants were out. A sow finding the doors open and attracted by the smell of the poultice came to devour it, whereupon the man was put into such a fright that his pains decreased that very day, and continued lessening by degrees and never returned." In this enlightened age, one can almost picture the excess flow of hormones from his adrenal glands stimulated by such excitement.

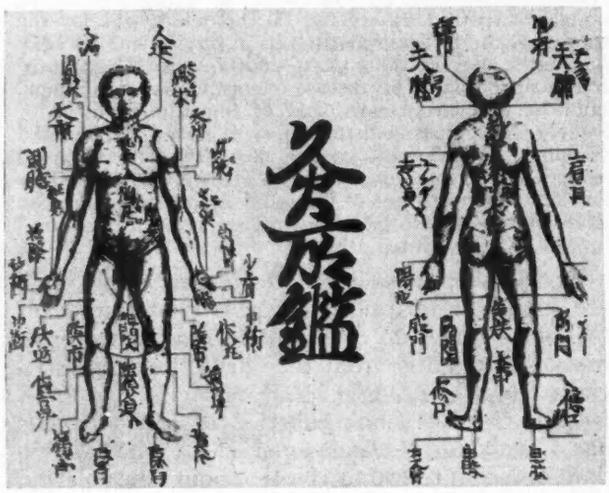

Fig. 2.—Indications of the places for applying the moxa. (From Kemfero, 1712.)

Boyle was also interested in the ancient belief of the transfer of disease, and notes that the gout is strangely eased if puppies lie with the person who has the gout, for they contract the disease, so as not to be able to run, but the patient hereby finds ease.

At this time there was published in London *The Haven of Health*, by Thomas Cogan, on the front page of which we read "Chiefly made for the comfort of students, and consequently for all those that have a care of their health, amplified upon five words of Hippocrates, Labour, Meat, Drink, Sleep and Venus."

In the epistle he writes "Wherefore I say to the gentleman who have the gout, that although the forebearing of wine and women and other things noisome in that disease do not utterly take away the gout, yet it will abate quality and abridge the pain and make it much more tolerable." He gives a vivid description of the hearty eating habits of the English and among other things recommends drinking before eating, for as he says "It is great cleanliness to wash the pot before we put in meat to be boiled." In his chapter on cheese, he points out that old and hard cheese is disallowed because it engenders melancholy. "Yet an old hard cheese is good for some things, for Galen showeth that an old cheese cut in pieces and sodden with the broth of a gammon of bacone and made in the manner of a plaster and laid to the joint where the gout is, will break the skin and dissolve those hard knots which the gout causeth."

In "The Lives of the Poets" by Samuel Johnson, we find another interesting character, tormented with headaches, blindness and the gout—Milton, the poet.

"Dr. Wright on a visit found him in a small house, he thinks but one room. He was sitting in an elbow chair, black clothes and neat enough, pale, but not cadaverous, his hands and fingers gouty and with chalk stones. Among other discourses he expressed himself to this purpose, that, was he free from the pain of gout, his blindness would be tolerable."

With such suffering one wonders why he did not write his famous sonnet "On His Gout" rather than "On His Blindness." But the torments of the gout may have been the inspiration for his description of the torments of Hell in "Paradise Lost," which he was writing at this time. However, it seems that many of his choicest years were employed in bitter wrangling, accusation and irascibility, so much so that after his death the Dean of Westminster, Dr. Sprat, refused his monument. The name of Milton was in his opinion "too detestable to be read on the wall of a building dedicated to devotion." It is interesting that Milton's son-in-law, Edward Phillips, was one who chronicled the last illness of Cromwell. It would seem that he died of malaria, but other historians are more explicit. "His Highness they say lay very ill of the gout and other distempers contracted by the long sickness of my Lady Elizabeth."

The 17th century would indeed be medically barren without the name of Thomas Sydenham, who first distinguished between gout and rheumatism, and well deserved the name of the English Hippocrates. His classical description of the gout, written in 1683, has never been surpassed, perhaps largely because of his own suffering from the disease.

In the preface to *A Treatise on the Gout and Dropsy*, he notes that the stress of writing his treatise occasioned the severest fit of gout he ever had. "For the gout constantly returned as often as I attempted to go on with the work." He also humorously remarks that having suffered from gout for 34 years, his observations on its cure would not bear very much weight. His consolation as a victim of gout was that "Kings, Princes, Generals, Admirals, Philosophers, and several other great men have thus lived and died, and that it destroys more rich than poor persons, and more wise men than fools."

Sydenham unfortunately believed that the final causes of disease could never be understood by the human mind. He noted the value of a milk diet in reducing an attack but on return to ordinary living, the gout returned with more violence than ever. As to liquors "They are better if weaker than wine," but as to water alone "I esteem it crude and pernicious and have found it so to my cost, but young persons may drink water with safety." He was opposed to purging, but was a great believer in exercise and for the gouty advocated horseback riding, "But if that cannot be used frequent riding in a coach answers almost as well."

He concludes his treatise by censuring other authors who through ignorance or knavery extravagantly extol the virtues of certain remedies. He admits, however, that such a remedy will be found hereafter which will betray the

ignorance of the theorists. *Nevertheless it must be admitted that as a highly respected physician, by his opposition to purging and hence the use of colchicum, Sydenham must take the responsibility for retarding the advance in treatment in gout.*

We enter the 18th century with none other than a gouty queen on the throne—Queen Anne, who reigned from 1702 to 1714. For those who would question the diagnosis, it must be remembered that Anne was sufficiently addicted to alcohol to be lampooned as "Brandy-faced-Nan." Winston Churchill in his life of Marlborough specifically states that she suffered from gout. Her last illness is described in the Sloane Manuscript, where we read "On Wednesday, December 23rd, her Majesty was very uneasy all night with the gout in her foot." She went on to die of erysipelas and apoplexy.

Also early in this century, tragedy overcame William Congreve, the well-known Restoration dramatist. He was described as an elegant minor poet, a gouty man-about-town and the gallant of a wealthy duchess. His death by accident is described by Samuel Johnson. Congreve sought relief from his gout at Bath, "but being overturned in his chariot, complained from that time of a pain in his side, and died January 29th, 1729."

At this time also lived Lord Chesterfield, who in 1726 took his seat in the House of Lords, which he playfully called "the hospital for incurables." It is one of the strange ironies of capricious fortune that he should have attained permanent fame from the very intimate personal letters to his son, never intended for publicity. He suffered from severe gout which may have tempered his letters, which in book form have been called "A Manual of Practical Morality," but which apparently offended the tastes of Dr. Johnson who stated that the letters "teach the morals of a whore, and manners of a dancing master."

Fig. 3. — The Treasury Spectre, or the Head of the Nation in a Queer Situation.

And now we turn to an important figure whose gout had a tremendous effect on British history—William Pitt, Earl of Chatham, who was born in 1708, at Golden Square, London.

Pitt was a manic-depressive; because of his gout this other weakness was euphemistically called gout in the head. In his early political life, hated by the King and with many enemies, he was out-manœuvred by his opposition but, as his country crashed from disaster to disaster, he achieved supreme power at the age of 49. England had been at war almost constantly for 23 years. Negotiations for peace with France were begun while Pitt was ill and unable to guide the nation. The government, wanting peace at any cost, regarded his illness with relief, but Pitt was not to be denied when faced with the destruction of his conquests.

Ill he might be, but he had the deep resources of strength which come to those who live constantly with sickness. He had himself carried to the House. He was dressed in black velvet which underlined his pallor. His legs were swathed in rolls of flannel, and the vast boot on his gouty foot was much in evidence. Standing was so painful to him that the House granted him the indulgence of sitting through part of his speech. He held the attention of the House for three and a half hours. At times the pain which he was suffering muddled his thoughts, but again and again the fire and passion flashed forth, ringing with the conviction he was never to lose, that the struggle between France and Britain was a mortal combat in which no compromise could succeed.

He was of course defeated and, after the Peace of Paris, resigned his office. The Peace of Paris sprang from a desire to avoid further costly burdens of war, and, as much of the expense of the Seven Years' War had been caused by extensive campaigns in America, it was felt that the American Colonies should be taxed for a war which after all had been fought in their in-

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terests. In 1765, the Stamp Act was passed. Pitt had disapproved strongly of this tax but he was too ill to make the journey to London, and scarcely a voice was raised against the bill. For some months he had been at Bath, brooding about the state of the nation, the folly of the American policy, and the iniquity of the Duke of Newcastle.

"Factions [he wrote to Shelburne] shake, and corruption saps the country to its foundation, while luxury emasculates and pleasure dissipates the understandings of men." On January 14, 1766, he rose before a crowded House to speak on the utter folly and absolute injustice of the Stamp Act.

Fig. 4.—Punch cures the gout. A Gillray cartoon published in 1799 by Humphrey, London. Three persons are seated in front of a bowl of punch. The gouty person says, "Punch cures the gout"; "And the colic," says his wife; "And the phthisis," says his friend.

"The Americans are the sons not the bastards of England. As subjects they are entitled to the common right of representation and cannot be bound to pay taxes without their consent. I rejoice that America has resisted." For the next month Pitt fought America's cause and the Act was repealed. Once again he became the popular idol of the people, and July 1766 saw him driving furiously down the Great West Road to answer the King's summons to form a ministry. For the first time Pitt was offered the sole direction of affairs foreign and domestic, but it was to prove a bitter fiasco. He collapsed under the strain of feverish work and recovered after two years to find that Townsend had betrayed him by placing a Colonial duty on tea and other commodities. (The entire income from these taxes was only £40,000 a year.)

Resentment and rebellion in America were the inevitable result. The year 1773 witnessed the famous Boston Tea Party, and Parliament had acted severely. Boston Harbour was closed and the offenders were removed to Nova Scotia for trial. Pitt was improving and in 1774 he felt well enough to intervene on behalf of America, but he was only a voice crying in the wilderness. However, another great gouty character, Benjamin Franklin, arrived on the scene as spokesman for the colonists, and Pitt and Franklin spent hours attempting to find some method by which the two countries might be reconciled. It would be interesting to reconstruct this historic scene: Pitt and Franklin, both victims of gout, seeking to find a solution to save America.

Following this consultation Pitt introduced a Bill which both Franklin and Jefferson thought might have been a suitable compromise, but it was rejected. After this bitter defeat Pitt scathingly denounced his colleagues. "The whole of your political conduct has been one continued series of weakness, temerity, despotism, ignorance, futility, negligence and the most notorious senility, irresponsibility and corruption. On reconsideration I must allow you one merit, a strict attention to your own interests."

Once more he collapsed and was forced to retire for two years. In 1777 he revived to find his inmost fears realized; war between America and Britain had broken out.

In the next year, it was obvious that he was a dying man, but in April when he heard that the Duke of Richmond proposed to press a motion for granting American independence, he resolved to make one more effort. It was the sense of shame which most deeply stirred him: "Shall a people that fifteen years ago, was the terror of the World now stoop so low as to tell its inveterate enemy, take all we have only give us Peace." He was carried insensible from the House and taken to Hays, his favourite home. There he died while his son William read to him from the Iliad of the death of Hector.

To quote from Trevelyan's *History of England*, "The gout, which he had been fighting with heroic constancy ever since his Eton days at last overcame the resistance of a lifetime. For months together he lay in brooding melancholy refusing to see his bewildered colleagues, fierce and unapproachable like a sick lion in its lair.

His ministry which had no principle of cohesion save his leadership staggered to ruin, carrying to limbo the last hopes of the country and the Empire." How unfortunate for England that colchicum was not more widely used in the time of Pitt. It is interesting to speculate whether or not the little autumn crocus might have prevented the Boston Tea Party, and the battle of Bunker Hill. Did Thomas Sydenham help to lose America by his opposition to a purging drug which contained the cure?

In 1796, Dr. William Falconer published his *"Dissertation on the Influence of the Passions upon Disorders of the Body,"* an essay for which he received the Fothergillian Medal.

In the chapter on podagra, "This complaint which is generally held to be excited by the passions of the mind in some instances may be cured by the same means." Like Boyle, he notes the value of fright. "A man disguised to represent a ghost took another labouring under a gouty paroxysm out of his bed and carried him down the stairs dragging his feet and legs which were the seat of his pain. The man thus treated immediately recovered the use of his limbs and ran up the stairs again with great swiftness and under the strongest impressions of terror. After this incident he lived many years free from any symptoms of gout." In another case history "A person who for forty years had been afflicted with the gout was condemned to capital punishment, and in consequence thereof led to execution. Just when he expected to die, he received an unhoped for pardon, which so affected his limbs as to restore them activity and strength, whereas before that even their use was nearly lost. This person as well lived many years totally free from the Gout."

About the year 1730, we find Thomas Gray reading Horace and Virgil at Eton. His lively and sensitive mind craved intellectual companionship, and Gray found a kindred spirit in Horace Walpole, the fabulously rich son of the prime minister. It seems a strange stroke of fate that both should eventually be afflicted with the gout. Their friendship had its periods of bitter resentment, but Gray sent all his poems to Walpole for criticism, including, bit by bit as it slowly grew to completion, *"Elegy in a Country Churchyard,"* and it was Walpole who arranged for their publication. Both were treated for the gout at Bath, and in "The Letters of Horace Walpole" we find an excellent description of the life in this gouty town.

"The waters agree with me and have bestowed such an appetite on me that I expect to return as fat as a hog. I am tired to death of the place and long to be at home —I have not yet been at the Ballroom or Pumproom for I steal my glass at The Cross Bath. We have all kind of folk here, Lord Chatham, The Chancellor, Lady Rockingham, Lady Scarborough, Lord and Lady Powis, Lord and Lady Spencer, Judges, Bishops and Lady Vane."

"My Lord President goes to the balls, but I believe had rather go to the Ale House. The Bath is sure of doing me some good for I shall take care of myself for fear of being sent hither again."

It was the Bishop Monk of Gloucester who said that Sydney Smith was given his appointment as a Resident Canon of St. Paul's Cathedral for being a "scoffer and a jester." How this great clergyman maintained his wit in the face of intolerable gout is difficult to imagine. It was Sydney Smith who divided humanity into three sexes, men, women and clergymen, and it was he who said of a stupid man, "he deserves to be preached to death by wild curates." It was probably indiscreet for a clergymen to say that "We have no amusements in England, but vice and religion," or to describe a friend's idea of Heaven as "eating *pâté de foie gras* to the sound of trumpets." In one of his letters to Lady Carlisle, on September 5, 1840, he writes: "What a very singular disease gout is, it seems as if the stomach fell down into the foot. The smallest deviation from the right diet is immediately punished by limping and lameness, and the innocent ankle and blameless instep are tortured for the vices of the nobler organs. A plum, a glass of champagne, excess in joy, excess in grief, any crime however small is sufficient for redness, swelling and large shoes. Gout is the only enemy that I do not wish to have at my feet." And in another letter "My breathlessness and giddiness are gone, chased away by the gout. If you hear of sixteen or eighteen pounds of human flesh, they belong to me. I look as if a curate had been taken out of me." But in many letters he praises the power of colchicum. In one to Lady Grey, "On Sunday, I was on crutches, utterly unable to put my feet to the ground. On Tuesday, I walked four miles, such is the power of colchicum."

The sixty years of the reign of George III were adorned by some of the greatest names England had ever known, but the commanding and representative personality of Samuel Johnson is better known and dearer to most of us than any other.

All his life Johnson was a keen amateur student of medicine, and took the greatest interest in his own ailments. His robust temperament made him a strong believer in drastic remedies, and no physician could give Johnson too violent a cure. He showed his displeasure of the cautious treatment of the great Heberden by referring to him as "timidorum timidissimus." He had another habit when ill of supplementing the efforts of his physician by strong measures of his own, and this ill-judged interference in the end cost him his life.

Boswell vividly describes their tour of the Hebrides and the island of Skye, where they were entertained for some days at Dunvegan Castle, the ancient seat of the MacLeods. It is not unnatural that at times their table talk drifted to Johnson's affliction, the gout. At supper Lady MacLeod mentioned Dr. Cadogan's book on *"The Gout,"* a current best seller. Mr. Johnson said " 'Tis a good book in general, but a foolish one as to particulars. 'Tis good in general as recommending temperance, exercise, and cheerfulness. 'Tis foolish as it says the disease is not hereditary, and one fit of the gout when gone is like a fever when gone." "But," said Lady MacLeod, "Dr. Cadogan does not practise what he teaches." Johnson replied "No man practises so well as he writes. I have all

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my life long been lying till noon, yet I tell all young men, and tell them with great sincerity, that nobody who does not rise early will ever do any good."

Johnson's health began to fail in 1782. "The gout has within these four days come upon me with a violence which I never experienced before. It made me helpless as an infant. I hope God will yet grant me a little longer life and make me less unfit to appear before him."

As his health failed he did a most unwise thing. Although he had at his command the skill

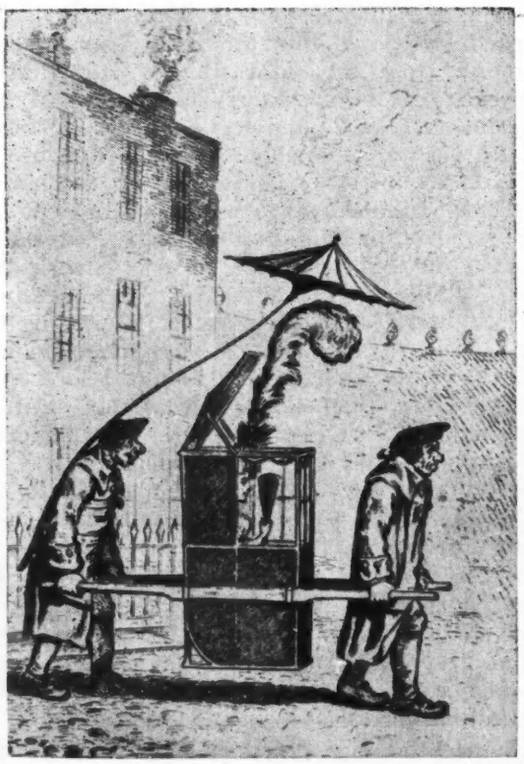

Fig. 5.—A modern Belle going to the Rooms at Bath.

of the ablest medical men in London—Heberden, Baker, Warren, Pepys and Brocklesby—he was persuaded by Boswell to consult by letter the great medical authorities in Edinburgh. He detailed the symptoms of his case to Cullen, Dick, Gillespie and Munro. The result was what one might expect. Johnson's time was largely employed in taking an incredible mixture of drugs. By November 1784, his dropsy assumed enormous proportions. Incisions were made in his legs to let out the water, but next morning Johnson ordered his servant to hand him a lancet, and with his own hand made the cuts deeper. He could not survive the loss of blood and died before the day was over.

To complete the 18th century, we must again return to Benjamin Franklin, who it is stated first brought colchicum to America, though we are unable to confirm this important historical step. The study of medicine was one of Franklin's chief interests, and one of the least known. Many medical men were among his most intimate companions and most valued correspondents.

In a letter to Alexander Small in 1780, he says, "You inquired about my gout and I forgot to acquaint you that I had treated it a little cavalierly in its last two excesses. Finding one night that my foot gave me more pain after it was covered warm in bed, I put it out of bed naked, and perceiving it easier, I at length fell asleep leaving it there till morning. The pain did not return, and I got through well." In another letter to John Paul Jones, "Be so good as to remember me affectionately to Mr. Wharton, and tell him that I am still in his gouty shoes which I have worn this week past, and thank him for the comfort of them."

Franklin was a sociable creature and loved cheerful companionship, and his household accounts speak of large and learned purchases of the best vintages of France. He tried hard to drink less wine, but in 1780 had a gouty spell which lasted six weeks, during which time, with a humour which the pain could not touch, he wrote his famous *"Dialogue with Gout,"* in which the malady tells him he deserves all his discomfort.

Later Franklin also suffered from the stone, and in his last summer became so emaciated from the use of opium that, as he said, "little remains of me but a skeleton covered with a skin." It was at this time that he wrote his famous statement "in this world nothing can be said to be certain except death and taxes." Nine days before his death he wrote to Thomas Jefferson, clearly and accurately telling him of the map which fixed the boundary between Maine and Nova Scotia. He died at 84 years of age.

As we enter the 19th century, we even find Mrs. Beeton, in her *"Household Management,"* treating the gout with all the assurance that she commands in coping with other household problems. In the section called "The Home Doctor," she wisely cautions temperance and suggests that the tincture or wine of colchicum be given every four hours.

The gouty attack is now seen to be well under control. In an essay read before the Royal College of Physicians, Sir Henry Halford, President of the College, states "There is no malady to which I am called upon to administer that I prescribe for with so much confidence in the resources of our art, as for the gout, formerly the *opprobrium medicorum*. My dependence is placed upon colchicum, for which I give the wine from the root." As he lectured he had specimens of colchicum and hermodactyl from Constantinople on the table before him.

Colchicum had come to stay. Baron Anton Stoerch had reintroduced the drug for dropsy and pleurisy, but the credit for reintroduction of its use in gout must go to a French army officer, Nicholas Husson, not a doctor, who concocted a panacea called *eau médicinale*. It rapidly became the chief constituent of many patent medicines, such as Wilson's Tincture and

Reynolds's Specific, which brought extravagant wealth to their vendors.

In 1848, Garrod presented his original observation that ever since has been a basic principle in the disease. He demonstrated an increased amount of uric acid in the blood of gouty subjects, and that colchicum did not influence the amount or excretion of uric acid, in spite of its beneficial effect. After 2,000 years of intermittent use, the mechanism by which colchicum cures the gouty attack still remains obscure.

A single reference might be noted in the 20th century, a study of British genius by Havelock Ellis, published in 1927, in which he states:

"There is, however, a pathological condition, which occurs in men of such pre-eminent intellectual ability, that it is impossible not to regard it as having a real association with such ability. I refer to gout."

"Moreover the eminence of these gouty subjects is as notable as their number. They include Milton, Harvey, Sydenham, Newton, Gibbon, Fielding, Hunter, Johnson, Congreve, the Pitts, Wolsey, Landor, Hamilton, and Charles Darwin, while the Bacons were a gouty family. It would probably be impossible to match the group of gouty men of genius for varied and preeminent intellectual ability, by any combination of non-gouty individuals on our list. It may be added that these gouty men of genius have frequently been eccentric, often irascible, choleric, and occasionally insane. This association of ability and gout," he continued, "cannot be a fortuitous coincidence. When the poison is in the victim's blood his brain becomes abnormally overclouded, if not intoxicated; when it is in his joints, his mind becomes abnormally clear and vigorous. Genius is not a product of gout, but it may be that the gouty poison acts as a real stimulus to intellectual ability and a real aid in intellectual achievement."

Gout as an arthritic problem has largely been conquered. The active principle of colchicum is now in a refined state in a pill. The excessive amount of uric acid in the blood may now be reduced by another pill.

Why was colchicum, used in the 6th century and nurtured through the dark ages, dropped from general use for hundreds of years when many historical figures were greatly in need of it? The answer to the mystery seems to lie partly in a confusion of botanical terms. A study of ancient medical books and herbals shows that the meadow saffron or colchicum was confused with the yellow saffron which belongs to another family and has no curative value; also, the violent and unpleasant effects caused by an overdose of colchicum had led to its removal from the ancient pills and mixtures.

It is sad to look back on the sufferings of so many creative and eminent people, but perhaps without the tempering influence of the gout we might have been deprived of Goethe's *Faust*, *Paradise Lost*, *Elegy in a Country Churchyard*, or even the Franklin stove.

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GENERAL PRACTICE

GENERAL PRACTITIONERS ON HOSPITAL STAFF

M. H. SMITH-WINDSOR, M.D.,
Saskatoon, Sask.

AT THE MARCH MEETING of the medical staff of St. Paul's Hospital, Saskatoon, a symposium dealing with the work of the members of the medical staff engaged in general practice was presented by Drs. M. H. Smith-Windsor, F. W. Rosher and M. H. Brook.

For the presentation, studies were made of the following:

1. The number of general practitioners on the staff and the number in the various departments. For this purpose, the staff roster for 1955 was reviewed by the record office.
2. The number of admissions by general practitioners in 1954.
3. The number of procedures carried out by general practitioners in the operating theatres, maternity department and emergency department.
4. The part taken by general practitioners in the teaching of nurses and interns.
5. The part taken by general practitioners on the various committees of the medical staff.

Figures were obtained through the supervisors of the various departments and the record office. Where applicable, comparison is made with the over-all picture in the department concerned.

Dr. Smith-Windsor dealt with the statistical side of the subject. The total staff (active, associate and courtesy) is 111, of whom 41 are general practitioners. In the department of medicine 16 out of 55 are general practitioners (plus 16 courtesy staff), in surgery 26 out of 54 (plus 7 courtesy staff), in obstetrics 23 out of 31 (plus 5 courtesy staff), and in ophthalmology and otolaryngology 2 out of 11 (plus 4 courtesy staff). The following are some statistics indicating the extent of general practitioner activity.

Admissions (1954)

Total admissions	8553	
Total number of staff members admitting patients	78	
Average admission	109.65	
Total number of general practitioners admitting patients	40	
Total number of their admissions	4303	
Average admission by G.P.	107.59	

Obstetrical Department (1954)

Total confinements	1380	
Total confinements by general practitioners	1128	(81.73%)

Operating Room (1954)

Total number of procedures	3804	
Total number of procedures by general practitioners	1245	(32.46%)

General Anæsthetics (1954)

Total number of general anæsthetics	2948	
Total number of general anæsthetics by general practitioners	1771	(60.07%)

Outpatient and Emergency Department (1954)

Total number of cases	5832	
Total number of cases attended by general practitioners	3170	(56.08%)

Teaching Programme—School of Nursing

Total hours of lectures (August 30, 1954 to April 30, 1955)	314
Total number of lectures	24
Number of general practitioners lecturing	4
Hours by general practitioners lecturing	46
Percentage of total hours	14.65%

Intern Teaching (Clinics and Lectures)

Hours of instruction	150
Number of clinicians	32
Number of general practitioner clinicians	9
Percentage of participation	39.1%

Procedures in X-ray Department (January 1955)

Total procedures requested	775
Total procedures requested by general practitioners	278
Percentage of total	36%

The foregoing figures indicate the extent of general practitioner activities in this hospital on a quantitative basis. Detailed examination of mortality and morbidity rates would provide a useful basis for appraisal of the quality of work done.

General practitioners are active in the work of the tissue, medical records, pharmacy, executive, admitting and credentials committees; on the subcommittees on intern teaching and constitution revision; and on the medical advisory board.

To ensure a continued place for the general practitioner on the medical staff, the draft of the new constitution includes provision for the establishment of a Department of General Practice as an administrative and educational department, whose members will have privileges and responsibilities in the various clinical departments.

In his presentation Dr. Rosher dealt particularly with the activities of the general practitioner in the outpatient department, illustrating the nature of such activities by reviewing the treatment of Colles' fractures during the year 1954. He stressed the part to be played by general practitioners in the "sorting out" of patients requiring inpatient care, and mentioned the economic factors involved in such activities.

Dr. Brook discussed the role of the general practitioner in the practice of medicine in the past and at present, and his probable role in this respect in the future.

Discussion which followed was concerned with the means by which general practitioners could progress in their activities in the hospital, with particular reference to work in surgery.

MEDICO-LEGAL

MISLAID FOREIGN BODIES DURING SURGERY
II. PACKING

J. H. B. HILTON, M.D.,* *Ottawa*

IN THIS SECOND of three articles dealing with mislaid foreign bodies during surgery, a case will be reported in which a sponge count was done, recorded and certified as correct, and yet surgical gauze was left in the patient's abdomen.

In 1951 this public-ward male patient was operated on in a large teaching hospital in one of our university cities. The operation was carried out by the surgical resident with a senior attending man assisting him. A retropubic prostatectomy was performed, two gauze packs six feet (180 cm.) in length being used to elevate and fix the prostate. After the prostatic capsule had been closed, the attending surgeon left the operating room, and the surgical resident completed the closure of the wound with a junior intern to assist him. The postoperative course of this patient was uneventful and he left hospital in the usual length of time. Almost a year later the senior attending surgeon who had been present and assisted at the operation was notified by this patient's family doctor that the man was having a febrile illness with pelvic pain and pus in his urine. This illness had been going on for at least a month when the attending physician was called to see him. The doctor found that the patient had begun to pass some gauze packing by rectum. About five feet of this packing was removed.

Very shortly after this the attending surgeon received a lawyer's letter asking for an explanation of this occurrence. Almost literally, there was no explanation. A final settlement was eventually made with the patient for $3,600. The total cost to the Canadian Medical Protective Association for this whole case amounted to about $4,500.

This incident brings up two points of interest and importance. The first is that in this instance a sponge count was done and was reported as correct. However, the two pieces of packing were not recorded, so that when the sponge count was reported as correct the surgeon was given the erroneous impression that all gauzes and sponges were safely out of the operation site. This simply emphasizes the fact that anything used for packing or drainage which must be placed within the operative site should be remembered, recorded and checked before the operation is finished. Any packing which must be left in for a time following an operation should be recorded at the time of operation, with the length and type of packing used. If there is more than one piece, the number of pieces with their length and size should be recorded. In this way, when such packing is removed the surgeon can be sure that all pieces and all of each piece has come safely out of the operative site.

The other point of interest is the division of responsibility in a case such as that described above. It will be noted that the surgical resident carried out the operation, assisted by the senior attending surgeon. In the final analysis, however, under such circumstances, where the senior or resident is in a sense apprenticed to the attending man, the attending surgeon, although he is actually assisting, is in reality responsible for the conduct of the whole operation. It is therefore his responsibility to be sure that no sponges or gauze or other foreign bodies are left behind when the operation is completed. This division of responsibility would not be the same should one surgeon of equal standing and training be assisting another.

This article is a reminder that, even though sponges are counted and are all accounted for, such sponge counts do not include gauze packing. Packing must be recorded as well if accidents such as this are to be avoided.

*Assistant Secretary-Treasurer, Canadian Medical Protective Association.

MEDICAL SOCIETIES

ASSOCIATION DES MEDECINS DE LANGUE FRANCAISE DU CANADA

Nous publions ci-dessous le programme scientifique du XXVe Congrès de l'Association des Médecins de Langue Française du Canada, qui aura lieu a l'hôtel Sheraton-Mont-Royal, Montréal, les 21, 22, 23, 24 septembre:

Séances plénières
Salle Champlain

Jeudi, le 22 septembre

Avant-midi –

9 h. à 9 h. 20 – Les troubles de la coagulation sanguine. – Docteur Léopold Long.

9 h. 20 à 9 h. 40 – Cytopénie immunologique. – Docteurs J.-M. Delage et Léo Gauvreau.

9 h. 40 à 10 h. 40 – Symposium sur l'occlusion intestinale.

9 h. 40 à 10 h. – L'aspect médical. – Docteur Roger Dufresne.

10 h. à 10 h. 20 – L'aspect radiologique. – Docteur A. Vallée.

10 h. 20 à 10 h. 40 – L'aspect chirurgical. – Docteur M. Lamoureux.

10 h. 40 à 11 h. – Considérations sur la détermination du volume sanguin et sur ses applications cliniques. – Docteur Albert Bertrand.

11 h. à midi – Forum sur le prurit ano-vulvaire. – Docteur Albéric Marin, animateur.

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Docteurs Paul Poirier, Raymond Simard, Ivan Vallée, Réginald Archambault et Fernand Côté.

Après-midi —

2 h. à 3 h. 20 — Symposium sur l'ictère.
2 h. à 2 h. 20 — L'aspect médical. — Docteur Sylvio Leblond.
2 h. 20 à 2 h. 40 — L'aspect chirurgical. — Docteur Wilfrid Caron.
2 h. 40 à 3 h. — L'aspect radiologique. — Docteur J.-H. Lapointe.
3 h. à 3 h. 20 — L'aspect biochimique. — Docteur Henri Marcoux.

3 h. 20 à 3 h. 40 — Traitement chirurgical des ictères par obstruction chez le nourrisson. — Docteur Paul-Louis Chigot (délégué français).

3 h. 40 à 3 h. 55 — *Visite des expositions scientifique et commerciale.*

4 h. à h. 20 — La recherche est-elle possible dans une institution canadienne-française? — Docteur Paul David.

4 h. 20 à 4 h. 40 — Les anémies. — Docteur Léopold Morissette.

4 h. 40 à 5 h. — De l'utilité de l'épreuve de Master dans l'angine de poitrine. — Docteurs R. Lessard et G. Saulnier.

5 h. à 5 h. 20 — Le volvulus chronique du sigmoïde. — Docteur L.-P. Mousseau.

5 h. 20 à 5 h. 40 — Le côlon irritable. — Docteur Yves Chaput.

5 h. 40 à 6 h. — *Titre à venir.* — Docteur Pierre Maurice (Paris).

Vendredi, le 23 septembre

Avant-midi —

9 h. à 10 h. — L'examen du sein (film sonore et en couleurs). Commentaires sur les dysplasies mammaires. — Docteur François Archambault.

10 h. à 10 h. 15 — *Visite des expositions scientifique et commerciale.*

10 h. 20 à 10 h. 40 — L'orientation des recherches en microbiologie à l'Université de Montréal. — Docteur Armand Frappier.

10 h. 40 à 11 h. — La poliomyélite. — Docteur V. Pavilanis.

11 h. à midi — Symposium sur la psychiatrie.
11 h. à 11 h. 20 — Les troubles caractériels et du comportement chez l'enfant. — Docteur J.-E. Marcotte.
11 h. 20 à 11 h. 40 — Les psycho-névroses. — Docteur François Cloutier.
11 h. 40 à midi — La psychanalyse. — Docteur J.-B. Boulanger.

Après-midi —

2 h. à 2 h. 20 — Le cancer expérimental. Orientation et appréciation des acquisitions récentes. — Docteur A. Cantéro.

2 h. 20 à 2 h. 40 — La fièvre rhumatismale. — Docteur J.-M. Beauregard.

2 h. 40 à 3 h. — La néphrite aiguë. — Docteur Roland Dussault.

3 h. à 3 h. 20 — Recherches à l'Institut Lavoisier. — Docteur Fernand Grégoire.

3 h. 20 à 3 h. 35 — *Visite des expositions scientifique et commerciale.*

3 h. 40 à 4 h. 40 — Symposium sur la stérilité.
3 h. 40 à 4 h. — Spermatogénèse chez les primates. — Docteurs C.-P. Leblond et Y. Clermont.
4 h. à 4 h. 20 — Chez la femme. — Docteur Roland Simard.
4 h. 20 à 4 h. 40 — Chez l'homme. — Docteur Jean Grignon.

4 h. 40 à 5 h. — Métabolisme du phosphore à haute énergie chez le rat âgé. — Docteur Eug. Robillard.

5 h. à 6 h. — Forum sur la pathologie intra-thoracique. — Docteur Jules Prévost, animateur.
Docteurs Paul Robert, J. Bruneau, Armand Trépanier, Réginald Johnson, Fernand Grégoire, André MacKay.

8 h. 30 — Séance publique du Comité d'Economie médicale de l'Association à laquelle tous les congressistes sont invités.

Samedi, le 24 septembre

Avant-midi —

9 h. à 9 h. 20 — La maladie de Ménière. — Docteur Fernand Montreuil.

9 h. 20 à 9 h. 40 — La physio-pathologie du choc. — Docteur G.-A. Bergeron.

9 h. 40 à 9 h. 55 — *Visite des expositions scientifique et commerciale.*

10 h. à 11 h. 40 — Symposium de pédiatrie.
10 h. à 10 h. 20 — Pneumopathies aiguës de l'enfance. Pneumonites et pneumonoses. — Docteur Paul Letondal.
10 h. 20 à 10 h. 40—L'état actuel des maladies infectieuses de l'enfant. — Docteur Henri Charbonneau.
10 h. 40 à 11 h. — Tuberculose de l'enfant. — Docteur Albert Guilbeault.
11 h. à 11 h. 20 — L'état actuel de l'alimentation chez le nourrisson. — Docteur A. Royer.
11 h. 20 à 11 h. 40 — Nouveautés et notions courantes en chirurgie infantile. — Docteur Claude Bertrand.

11 h. 40 à midi — Hépatite à virus; hépatose au Largactil. — Docteur L.-C. Simard.

Après-midi —

2 h. à 3 h. 20 — Symposium sur le traitement du goitre et de l'hyperthyroïdie.
2 h. à 2 h. 20 — L'aspect médical. — Docteur Alf. Cléroux.
2 h. 20 à 2 h. 40 — L'aspect radio-actif. — Docteur Maurice Bélisle.
2 h. 40 à 3 h. — L'aspect chirurgical. — Docteur G.-E. Cartier.
3 h. à 3 h. 20 — L'aspect radio-thérapeutique. — Docteur Jean Michon.

3 h. 20 à 3 h. 40 — A propos de cinq cas d'adénome parathyroïdien opérés. — Docteur Paul-Louis Chigot (délégué français).

3 h. 40 à 4 h. — L'organisation, les contributions et les possibilités d'un département de recherches cliniques dans un centre médical canadien-français. — Docteur Jacques Genest.

4 h. à 4 h. 20 — Les hémorragies ante et post-partum. — Docteur F.-X. Demers.

4 h. 20 à 4 h. 40 — Choix de l'opération dans la cure du cancer recto-sigmoïdien. — Docteurs François Roy et Rosaire Voyer.

4 h. 40 à 6 h. — Forum sur les abus de la cortisone, des hormones et des antibiotiques. — Docteur C.-E. Grignon, animateur.
Docteurs Paul Dumas, André Leduc, Georges Hébert, Charles Ouimet, Georges Leclerc.

Sections

Jeudi, le 22 septembre

Anesthésiologie (Salon D) — A.M. et P.M.

Vendredi, le 23 septembre

Pédiatrie (Salon A) — A.M. et P.M.
O. R. L. et Ophtalmologie (Salon B) — A.M. et P.M.
Hygiène (Salon C.D.E.) — A.M. et P.M.

Samedi, le 24 septembre

Obstétrique (Salon A) — A.M. et P.M.
Radiologie (Salon D) — A.M. et P.M.

Les travaux présentés aux séances de ces sections seront inscrits dans le programme du congrès, distribué aux congressistes.

McINTYRE-SARANAC CONFERENCE ON OCCUPATIONAL CHEST DISEASE

The first joint meeting of these two institutions was held earlier this year at Saranac Lake, N.Y. It is interesting to trace the diverse origin of these pioneer facilities engaged in research into the pneumoconioses. The McIntyre Research Foundation is a Canadian enterprise and was originally established as McIntyre Research Limited to develop the aluminium therapy of silicosis, initiated by Dr. W. D. Robson and the late J. J. Denny, plant physician and engineer respectively of McIntyre Porcupine Mines Ltd. In 1946 the Foundation was established, with a charter membership of 10, as a non-profit corporation to carry on research and investigation in connection with the prevention, mitigation and eradication of industrial diseases. Initially research was concerned with the pathogenesis of silicosis; this was followed by clinical studies on the therapeutic use of aluminium on established cases of silicosis. A field unit was later established to study pulmonary function as revealed in pre-employment medical examination of applicants for work in occupations involving a dust hazard. Other associated investigations include sterno-vertebral measurements and their relationship to pulmonary disease. The effects of physical agents on dust and powder production, and pathological studies by means of large lung sections, have more recently been followed.

The Saranac Laboratory was founded by Dr. E. L. Trudeau in 1885 at his home. After various vicissitudes, including destruction by fire, a new laboratory was constructed in 1894 and this became the first institution specifically designed to study tuberculosis in the United States. In addition to extensive experimental work on tuberculosis the laboratory has systematically investigated the pneumoconioses and in particular has clearly demonstrated the phthisogenic quality of the quartz particle. Even antedating the Canadian publication of the prophylactic use of aluminium dust in silicosis, workers from the Saranac laboratory were examining the use of iron compounds for a similar purpose. In addition to its industrial hygiene service and physiological and radiological divisions, the Laboratory established a biochemistry department to assist in its investigation into berylliosis. This latter facility is presently conducting an enquiry into carcinogenesis and also inhalation experiments with a plastic dust.

At this year's meeting, Dr. G. W. H. Schepers' contribution on vascular changes in the lungs of pneumoconiotics attracted considerable interest. It was shown that the most marked effects are on the smaller vessels and comprise cellular and collagenous lesions of the capillaries of the alveolar wall. Damage to the arterioles and venules with perivascular deposition of pigments, macrophages and fibrocytes together with a variable degree of fibrosis was noted microscopically. The larger vessels may also demonstrate changes ranging from intimal atheroma to aneurysmal distension. These vascular lesions are in addition to the specific collagenous nodules found in established cases of silicosis. Dr. Schepers suggested that these vascular changes may be a factor in the pathogenesis of cor pulmonale.

From the Cleveland Clinic, Dr. H. S. Van Ordstrand and his co-workers recorded their experience using lung biopsy when other diagnostic procedures had yielded equivocal results. Over a five-year period, they have been able to establish a diagnosis in eleven borderline cases of occupational lung disease and have disproved 15 doubtful diagnoses.

Talcosis, the pneumoconiosis produced following inhalation of the talc powder used in the rubber industry, is also a dust hazard in mines and mills and was the subject of a report from Dr. M. Kleinfeld and associates from the Division of Industrial Hygiene, New York State Department of Labor. An account of present working conditions and dust concentrations in New York talc mines and mills was given and 32 cases of talcosis originally diagnosed 14 years previously were restudied. In view of the small size of the sample no specific conclusions could be drawn from the findings. The clinical picture most commonly seen was found to include emphysema, basal râles, diminished chest expansion and clubbing. Characteristic chest x-ray findings were a diffuse infiltration of the basal and midlung fields. Although the dust extraction has been improved in many work-places there has not been a corresponding retrogression of the pathological picture even on retirement. Dr. A. I. G. McLaughlin, H. M. Inspector of Factories, traced the origin and evolution in the United Kingdom of factory legislation designed to protect the worker in occupations involving dust hazards. It was shown that despite these measures and the combined efforts of physicians and scientists, the deaths from pneumoconiosis have continued to rise. This was due, in the opinion of the author, partly to improved methods of diagnosis and partly to the introduction of speedier and dustier machines with a corresponding lag in dust control methods.

CANADIAN PSYCHOANALYTIC SOCIETY

On February 15, 1955, the Canadian Psychoanalytic Society and the Société médicale de Montréal held their first joint meeting at the Hôtel-Dieu Hospital. The following papers were presented: "What is Psychoanalysis? Who are Psychoanalysts?" by Dr. J. B. Boulanger; "Indications for Psychoanalytic Therapy," by Dr. J. P. Labrecque; "Co-operation of Physician and Psychoanalyst," by Mr. A. Lussier; "Neurobiology and Psychoanalysis," by Dr. M. Prados. Drs. W. C. M. Scott, R. Amyot, J. Saucier, P. Larivière, L. Larue and F. Cloutier took part in the discussion.

At the Society's Scientific Meeting, held in Montreal on February 19, Dr. Bertram Lewin, of the New York Psychoanalytic Institute, spoke on "Dream Psychology and the Analytic Situation."

CANADIAN SOCIETY OF OBSTETRICIANS AND GYNÆCOLOGISTS

The Society of Obstetricians and Gynæcologists of Canada will hold their Annual Meeting at the Manoir Richelieu, Murray Bay, Quebec, on June 8, 9 and 10, 1956.

POSTGRADUATE COURSES

Symposium on Medical Practice: The Ontario Chapter of the College of General Practice and Lederle Laboratories. Royal York Hotel, Toronto, September 22.

Postgraduate Course: St. Paul's Hospital, Vancouver, B.C., October 27-29.

Medical Alumni Postgraduate Course: Sunnybrook Hospital, Toronto, October 13 and 14.

Refresher Course: Royal Victoria Hospital, Montreal, November 21-26.

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CORRESPONDENCE

BARBITURATE AND MORPHINE ANTAGONISTS

To the Editor:

It was with great interest that we read the Editorial Comment on barbiturate and morphine antagonists in the July 15 issue of *The Canadian Medical Association Journal.*

Recently, we obtained a small supply of Megimide through the courtesy of the manufacturers. The Megimide was used in six cases undergoing elective surgical procedures. Sodium Pentothal was employed as the main agent; in some cases alone, in others with nitrous oxide and succinyl choline. Electroencephalogram recordings were made in three cases during the operations and subsequently, to record the anæsthetic levels.

In no case was the "awakening time" appreciably hastened by Megimide. All the patients lapsed back to sleep. In those patients receiving the larger doses of Sodium Pentothal, and consequently the larger amount of Megimide, the sleeping time was longer than one would expect with similar doses of Sodium Pentothal alone. Our findings thus differ from that of Harris.[1] From our limited observations, we gained the impression that Megimide has an action somewhat akin to the analeptics. We have not as yet employed Megimide combined with Daptazole, as described by Shaw and Shulman.[2, 3]

Possibly, Megimide and Daptazole will take their place in the armamentarium of barbiturate and morphine antagonists. However, we feel that an insufficient number of controlled studies have been published to evaluate their true worth. A cautious approach to any new drug is always essential.

REFERENCES

1. HARRIS, T. A. B.: *Lancet,* 1: 191, 1955.
2. SHAW, F. H. *et al.*: *Nature,* 173: 402, 1954.
3. SHAW, F. H. AND SHULMAN, A.: *Nature,* 175: 388, 1955.

Department of Anæsthesia,
University of Alberta Hospital,
Edmonton, Alta.,
July 30, 1955.

E. A. GAIN, M.D.
S. G. PALETZ, M.D.

Dr. T. A. B. Harris was asked to comment on Dr. Gain's letter. Part of his comment is reproduced below.

Dr. Gain's results are so contrary to our experience that I can only surmise that he is using too little Megimide, too slowly. The last case of barbiturate overdose that I had to deal with before my holiday may illustrate this point. It was estimated that this subject had taken 60 grains of Sodium Amytal by mouth with some whiskey.

This man, aged 22 years, was brought to Guy's Front Surgery at *5.30 p.m. on August 2, 1955.* He was comatose with small equal pupils not reacting to light. There was no sign of injury. After examination, he was given nikethamide 4 ml. and then picrotoxin 6 mg. and was admitted to Mary Ward as a probable case of barbiturate overdose. Here oxygen therapy and analeptics (I cannot find details) were given without material benefit, and I was telephoned for at my home and saw him at 8.30 p.m. By then, one capsule of Amytal, 3 grains, had been found in his pocket.

On examination I found a deeply comatosed man who, in spite of oxygen through a BLB mask, was cyanosed. There were no signs of injury. His respiratory rate was 10 per minute; breathing was shallow, moist and bubbly. The eyeballs were fixed in the mid-line, pupils small and not reacting to light. The limbs were flaccid; no reflexes could be elicited. His pulse rate was 130. The systolic blood pressure was 55 mm. Hg.; diastolic pressure could not be measured.

He was insufflated with oxygen and the colour improved; 200 mg. of Megimide was given intravenously as rapidly as a large bore needle (10 gauge) allowed. His eyelid reflex returned in 45 seconds. The respiratory rate rose to 15: breathing deepened and the cheeks flushed up. The forearm flexed. The pulse rate fell to 110 and the blood pressure rose to 70/45 within three minutes.

Three minutes later another 200 mg. of Megimide was given at the same rate. He coughed and spat out his airway, made inarticulate noises and flexed his arms and legs. Within five minutes he had succeeded in clearing his larynx and posterior pharynx of accumulated irritating mucus. His pupils reacted to light, his pulse rate was 100 and his blood pressure was 85/50 mm. Hg. He could now oxygenate himself, adequately breathing air.

He had obviously reached a safe state and I left for home at 9.30 p.m. leaving instructions for a further 200 mg. of Megimide to be given if and when narcosis began to significantly deepen. (This is usual in my experience after very large dosage.) Accordingly the house physician gave another 200 mg. of Megimide at 11.30 p.m. The subject reawakened, mumbling speech was detected and he moved round in bed mumbling for the rest of the night, becoming progressively more coherent.

I saw him at 8.30 a.m. the next morning (August 3, 1955). He was sitting up in bed, smoking a cigarette and talking to anyone who would listen to him. He was observed for the rest of that day and discharged on the next day, August 4, 1955, to be interviewed by the police.

The first 80 cases I reported were all of a type, light thiopentone anæsthesia. Since then, Megimide has been used for a variety of cases and for 20 (circa) barbiturate suicides. We have had no failures to date and, when correctly used, results are obtained akin to the case I have outlined above. In this case, as you will note, therapy consisted solely of oxygen and Megimide; to me this is significant. Everything I have seen to date suggests, not an analeptic action but antagonism. Much pharmacological and biochemical work must be done before one can say "specific antagonism" but that is the way it looks clinically.

Guy's Hospital,
London, S.E.1,
August 23, 1955.

T. A. B. HARRIS, M.D., F.F.A.R.C.S.

DISTENSION OF THE ŒSOPHAGUS

The differential diagnostic problem between œsophageal and cardiac pain has been studied by Baylis, Kauntze and Trounce. A balloon was inflated in the lower œsophagus in eight normal subjects and in three with coronary artery disease, and the results were carefully studied clinically and by radiography and electrocardiography. The induced œsophageal pain differed from the pain of cardiac ischæmia in many respects, and no effect was induced electrocardiographically even in the cardiac patients. Atropine was found to have no analgesic effect upon the pain whereas amyl nitrite abolished it through temporary inhibition of œsophageal contraction induced by the distension.

The authors are of the opinion that the electrocardiogram offers the most reliable means of distinguishing between œsophageal and cardiac pain.—Baylis, J. H., Kauntze, R. and Trounce, J. R.: *Quart. J. Med.*, 24: 143, 1955.

ABSTRACTS *from current literature*

MEDICINE

Observations on the Pathogenicity of Isoniazid-Resistant Mutants of Tubercle Bacilli for Tuberculous Patients.

OESTREICHER, R. ET AL.: AM. REV. TUBERC., 71: 390, 1955.

It is well established that isoniazid-resistant mutants of tubercle bacilli have diminished pathogenicity for guinea-pigs. There is a high incidence of isoniazid-resistant mutants which can be isolated *in vitro* from isoniazid-susceptible populations of tubercle bacilli, as well as from many tuberculous patients treated with this agent. In spite of this fact, there are reports indicating that in miliary tuberculosis "relapse" under treatment with isoniazid alone is very rare. For these and other reasons, the authors considered it necessary to examine this problem, in order to derive from the available clinical material an approximate answer to the question of pathogenicity of isoniazid-resistant tubercle bacilli for human beings—in particular, for those who are already tuberculous.

Forty-five patients were selected for this study from the adult medical service and the follow-up department of the National Jewish Hospital, Denver, over a period of 2½ years. All these patients had undergone prolonged administration of isoniazid, preceded by treatment with either streptomycin, PAS, or viomycin or combinations of these agents. All patients had persistently positive sputum specimens containing large numbers of mutants of typical mammalian-type tubercle bacilli resistant to at least one mg. of isoniazid per ml. of medium during an observation period of not less than six months. Despite the presence of these large numbers of isoniazid-resistant mutants, treatment with *isoniazid alone* was continued in daily dosage of 4 to 16 mg. per kg. during the entire period of observation, with a few exceptions.

During this period of observation, numerous examinations were carried out, both clinical and laboratory, which might be expected to show whether the disease was progressing, retrogressing or remaining stationary. These examinations included roentgenographic studies, clinical observations, measurement of erythrocyte sedimentation rate and determination of body weight.

The results indicated that, under these conditions, new lesions of progressive tuberculous disease *failed to develop* in any except possibly one of these patients. The authors interpret these experiences as indirect evidence that the pathogenic potentialities of most isoniazid-resistant mutants of typical mammalian-type tubercle bacilli are strictly limited in an important manner for most tuberculous patients. S. J. SHANE

Lung Biopsy.

EFFLER, D. B. ET AL.: AM. REV. TUBERC., 71: 668, 1955.

The patient with bilateral diffuse pulmonary disease has, in the past, been considered as presenting a diagnostic problem entirely for the internist. However, all too frequently in such cases, specific diagnosis has been impossible, and several procedures have been devised in an effort to obtain additional information. These include, in particular, needle biopsy and scalene node biopsy.

Needle biopsy of lung tissue has been used for years, but has never gained wide acceptance because of its obvious danger and the lack of precision inherent in the procedure. Scalene node biopsy enjoys widespread popularity and is a reliable method of diagnosis in selected cases. In general it offers less than a 50% yield in diagnosis, and therefore does not approach the ideal in efficiency.

The writers have employed a technique of lung biopsy for a period of five years, and have been favourably impressed by the results. They describe their procedure in this paper and outline their results in 65 cases. Precise diagnosis can be made by this procedure in cases of disseminated pulmonary disease in a much larger percentage of cases than is possible with scalene node biopsy. The procedure is considered to be without danger and without significant morbidity.

There are two indications for lung biopsy: in diffuse pulmonary disease in which all reasonable studies have been exhausted and the diagnosis has not been established, and in selected cases in which the possible medico-legal occupational disease aspect may be of importance. S. J. SHANE

Idiopathic Pleurisy with Effusion, Presumably Tuberculous.

STEAD, W. W., EICHENHOLZ, A. AND STAUSS, H.-K.: AM. REV. TUBERC., 71: 473, 1955.

This report concerns the clinical, operative, and pathological findings in a group of 24 patients explored surgically within a few months of acute pleurisy with effusion. Of these 24 cases, 15 were tuberculous and 9 non-tuberculous. The findings shed light upon the pathogenesis of tuberculous pleurisy with effusion, while the findings in some of the patients who had no evidence of tuberculosis are of secondary interest.

The pleura was thick, fibrous and granulomatous in the 15 tuberculous patients. A definite parenchymal focus was found in 12 of the 15, and multinodular tuberculosis in 7 patients. Pleurisy was apparently caused by actual rupture of a caseous parenchymal nodule into the pleural space.

This provides a satisfactory explanation for the development of pulmonary tuberculosis within five years of a pleural effusion, since it appears clear that the pleuritis is secondary to caseous tuberculosis within the lung. Surgical exploration allowed an accurate appraisal of the extent of the tuberculosis. Many of the pulmonary lesions were not even visible on retrospective study of the roentgenograms.

Seven of the non-tuberculous cases were characterized by long-continued formation of free pleural fluid, apparently on a hydrodynamic basis. The lower half of the lung was trapped and compressed by a tough fibrous "peel." There were two cases of fibrothorax following intrathoracic hæmorrhage. The authors feel that every patient with unexplained exudative pleurisy should be carefully studied for the presence and extent of tuberculosis so that appropriate therapy may be given. These studies should include planigraphy. If the illness does not follow the typical course for primary tuberculous effusion, an exploratory thoracotomy is warranted for more accurate diagnosis. Because of the underlying pulmonary tuberculosis, a minimum of eight months of treatment is advisable, even for the typical case of primary effusion. S. J. SHANE

Diffuse Indolent Pulmonary Tuberculosis.

BUECHNER, H. A. AND ANDERSON, A. E.: AM. REV. TUBERC., 71: 503, 1955.

The authors describe a diffuse indolent form of pulmonary tuberculosis, designated in the past as "chronic productive tuberculosis." For many years, the treatment of this form of tuberculosis has presented an unusually difficult problem. During the pre-streptomycin era it was repeatedly emphasized that bed rest, sanatorium care and collapse measures had little effect on the course of the disease; and it was generally recommended that the patient be allowed to lead his usual life, entering the sanatorium only when periodic exacerbations occurred. It was even stated that it was "almost criminal

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to confine the victim of this form of tuberculosis in a sanatorium, where little could be done to alter the gradual progression of pulmonary lesions." However, the eventual prognosis was poor, and the patient usually succumbed to an acute caseous tuberculous pneumonia, or died from emphysema, fibrosis, anoxæmia and cardiac failure.

The introduction of specific antimicrobial agents has changed concepts of management and prognosis in this form of the disease. Although the response of diffuse indolent pulmonary tuberculosis to antimicrobial agents is not so dramatic, some improvement can be expected in almost every case in which antimicrobial agents are employed. The authors combine antimicrobial therapy with short periods of bed rest, pneumoperitoneum being frequently utilized as an adjuvant measure.

It is emphasized that this therapy will result only occasionally in marked clearing of the pulmonary lesions; however, some improvement, or at least an arrest of the progression of the disease, can nearly always be expected. While this falls far short of an ideal result, it affords promise, at least, of avoidance of the crippling effects of late emphysema and fibrosis, and improves the general prognosis.

The authors' conclusions are based on results obtained with streptomycin and PAS; they feel that the use of isoniazid may brighten the outlook further.

S. J. SHANE

Tuberculous Meningitis: Diagnostic and Prognostic Significance of Spinal Fluid Sugar and Chloride.

GIERSON, H. W. AND MARX, J. I.: ANN. INT. MED., 42: 902, 1955.

It is generally agreed that the typical spinal fluid in tuberculous meningitis reflects an elevated pressure, a moderate pleocytosis, an increased protein content and a decline in the sugar and chloride values. Since some of these changes are considered to be non-specific, the authors carried out a study to assay the diagnostic and prognostic significance of these determinations, and to ascertain the necessity or desirability of examining both these factors, when the clinician is called upon to diagnose and treat meningeal tuberculosis.

The study included 231 cases of tuberculous meningitis, in which spinal fluid was carefully studied, particularly during the first few days of hospitalization, that is, the diagnostic period. Both sugar and chloride content were depressed in most instances, but in a significant number of cases one or the other was normal at the time of the initial examination, and remained so throughout the diagnostic period. Sugar levels failed to reflect the meningeal tuberculosis more often than did the chloride levels. In other words, neither the spinal fluid glucose nor the chloride provided a sensitive prognostic index. However, the chloride level was slightly more reliable; and the authors recommend that chloride determinations be part of the routine spinal fluid analysis in tuberculous meningitis.

S. J. SHANE

Cerebral Thrombosis in Young Adults.

BERLIN, L., TUMARKIN, B. AND MARTIN, H. L.: NEW ENGLAND J. MED., 252: 162, 1955.

Premature vascular degeneration, with resultant thrombosis of cerebral vessels, is a more common cause of acute neurological syndromes in young adults than is generally recognized. In 13 such cases, the age of the patients varied from 18 to 34 years, with the exception of one patient aged 55 admitted with a mild cerebrovascular accident but included in this present series because of previous attacks 34 and 32 years before. Only one death occurred. Thorough investigation revealed no other apparent cause in any case apart from presumed arteriosclerosis.

The experience of the authors leads them to the opinion that "strokes" in the younger age group are less severe and carry a much better prognosis than in the older patients.

NORMAN S. SKINNER

Diagnosis and Management of Biliary-Tract Disease.

ZOLLINGER, R. M., BOLES, E. T. AND CRAWFORD, G. B.: NEW ENGLAND J. MED., 252: 203, 1955.

This is an excellent summary of a very important subject and incorporates the wide experience of the authors. They point out that the accuracy of diagnosis of gallbladder disease by cholecystography is very high; nonvisualization should be checked by a repeat examination with an increased oral dose of opaque medium, but radiographic findings such as poor filling, poor emptying, and abnormal size and shapes of the gallbladder are not in themselves indications for gallbladder surgery. Silent stones should be removed in the young and middle-aged, but a conservative policy is warranted in old people with relatively short life expectancy. Cholecystectomy is generally indicated when gallstones are found in association with symptomatic cardiac disease, pancreatitis or duodenal ulcer.

Acute cholecystitis calls for immediate hospitalization with close observation and adequate hydration of the patient. If the patient steadily improves, operation is postponed until the patient is ambulant and taking food well. Failure to improve, or an increase in the severity of symptoms, calls for immediate surgery.

Common duct stones are present in about 20% of patients with cholelithiasis and are more common the older the patient. No surgeon should attempt cholecystectomy unless he is prepared to explore the common duct.

In the presence of jaundice, biliary tract surgery should be delayed until adequate clinical investigation has been carried out along with dietary preparation and replacement of any blood-volume deficit.

NORMAN S. SKINNER

Non-specific Enterocolitis.

COOKE, W. T. AND BROOKE, B. N.: QUART. J. MED., 24: 1, 1955.

Under the term non-specific enterocolitis the authors report a condition often incorrectly diagnosed as either regional ileitis or chronic ulcerative colitis. The presenting symptom in all cases is diarrhœa, which may be continuous or intermittent, the latter cases particularly being confused with ulcerative colitis.

Non-specific enterocolitis starts in the small bowel; the colon may be involved secondarily, usually the right colon but in severe cases the entire colon. Excessive fat is present in the stools while blood and pus are inconspicuous or absent. Iron deficient anæmia is the rule and occasionally a macrocytic anæmia is present. Radiological examination will demonstrate the so-called "deficiency pattern" of small bowel abnormality; colonic changes also may be present but are predominantly right-sided and are the distal extension of the process arising in the small intestine. Pathologically, stenosis does not occur; changes are limited to the mucosa and consist of multiple, small superficial ulcers with areas of œdematous and intact mucous membrane between them.

The cause of non-specific enterocolitis is unknown. Therapy is indirect, aimed at correcting the anæmia and the deficiency state. Surgery is contraindicated; since it is primarily a small bowel disorder an enterostomy usually makes the situation worse. Resection of the involved small bowel and vagotomy have been tried but have yet to prove their worth.

Sixteen cases are described in detail. While many of the patients are carrying on essentially normally, seven have died.

NORMAN S. SKINNER

SURGERY

The Peritoneum . . . A Plea for a Change in Attitude Towards this Membrane.

WILLIAMS, D. C.: BRIT. J. SURG., 42: 401, 1955.

Another concept considered fundamental in abdominal surgery has been attacked from both clinical and experimental evidence: that raw surfaces should be peritonealized. As early as 1917, Corbett pointed out that adhesions do not form in the absence of inflammation. In 1932 Babcock expressed the opinion that after resections in the pelvis patients not undergoing peritonealization did better postoperatively. Brunschwig also advises against reconstruction of the pelvic peritoneum after pelvic evisceration. The very trauma of closing the raw surface causes more inflammation than would otherwise occur. Peritoneum is a mesothelium replaced very rapidly and should not be compared with epithelium, a highly specialized tissue.

Experiments on rabbits are described to show the regeneration of epithelium in two to five days, and the behaviour of ligated stumps of bowel. These lend support to the view that a raw area in itself will not cause adhesion formation, and that a primarily inflamed tissue must produce inflammatory changes in any contiguous structure before an adhesion can form. Infection is by far the commonest cause of adhesion. BURNS PLEWES

Congenital Intestinal Atresia.

FEGGETTER, S.: BRIT. J. SURG., 42: 379, 1955.

During 15 years in Newcastle, congenital atresia or stenosis of duodenum or small intestine has been diagnosed with increasing frequency, and 35 cases are described. It probably occurs once in 2,500 live births. The only treatment is early operation. In hospitals where a pædiatrician has been attached to the maternity unit, diagnosis is usually made very early. Flat plate radiography of the abdomen in a newborn infant is usually enough for the diagnosis when the obstruction is suspected, but no objection is made to the use of thin barium emulsions.

At operation, the site of the lesion may be hard to demonstrate, for the bowel on either side of the atresia may be of about the same size. Gastroenterostomy or duodenojejunostomy is better than attempts to break down an occluding membrane.

The recovery rate in this series was 58%, much the best results occurring in cases of duodenal occlusion, where the rate was 70%. BURNS PLEWES

Primary Diverticula of the Duodenum.

WAUGH, J. M. AND JOHNSTON, E. V.: ANN. SURG., 141: 193, 1955.

In a series of 525 cases in which the diagnosis of duodenal diverticulum was made by clinicians at the Mayo Clinic, the 30 cases operated upon are reviewed. The concept that a primary diverticulum is a mucosal herniation through a weakness of the muscularis is confirmed. Radiologists find duodenal diverticula in 1 or 2%, and autopsists doing careful dissections in up to 14.5%.

Duodenal diverticula are seen more frequently the older the patient and most often on the medial aspect of the second portion. They are multiple in 26%. In 23% there were also diverticula of the small intestine, and in 45% diverticulosis of the colon. Complications due to inflammation—perforation with abscess or fistula—are rare. Occasionally a diverticulum causes obstruction of the pancreatic duct and pancreatitis. Obstruction of the common bile duct or of the duodenum is rare, as are ectopic glandular tissue and tumours.

Symptoms are difficult to evaluate: epigastric distress especially after heavy meals, relief by a flexed supine position, antispasmodics, belching or vomiting and so on. The incidence of exploration for diverticulum is now very low (about 2%), so that the feeling that diverticula do not cause symptoms is substantiated. Emphasis is placed on the importance of functional complaints in the differential diagnosis.

Two deaths and two complications followed diverticulectomy in these 30 cases, and nearly half the patients were not relieved of their symptoms. The results of operative treatment have been disappointing.
BURNS PLEWES

Classification of Retroperitoneal Tumours as a Guide in Clinical Diagnosis.

ENGEL, W. J.: A. M. A. ARCH. SURG., 70: 156, 1955.

Retroperitoneal tumours are usually palpable through the abdomen and may occur at any age. The retroperitoneal space lies between the diaphragm and the pelvic brim and the posterior peritoneum and the muscles of the abdominal wall. The classification suggested is under the following headings:

I. *Primary unattached tumours:* (a) Benign—chiefly from embryological remnants of the urogenital tract, also from adult tissue-fat, nerves, etc. (b) Malignant.

II. *Arising from organs in the retroperitoneal space:* (a) From kidney—benign: neoplasms, congenital, inflammatory, traumatic; malignant: renal cell, sarcoma, mixed tumours, renal pelvis. (b) From adrenal—medullary, cortical. (c) From pancreas—cysts, carcinoma.

III. *Arising in lymph nodes:* (a) Primary-lymphosarcoma, Hodgkin's, etc. (b) Metastatic—from testicle, ovary, etc. BURNS PLEWES

Acute and Chronic Cholecystitis.

MEAGHER, S. W. AND CAMPBELL, A. J. A.: NEW ENGLAND J. MED., 252: 615, 1955.

A practical study was made of 329 cases operated upon at the Boston City Hospital during 1951 and 1952 with a preoperative diagnosis of cholecystitis.

Of 99 cases diagnosed as acute cholecystitis 11 were found to have no gallbladder disease; there was no significant sex difference in frequency, and the age at which acute cholecystitis occurred tended to be older than for the group with chronic cholecystitis. The postoperative mortality was 7.9% of the entire number of cases of acute cholecystitis and 13% of those requiring emergency surgery.

Of 230 cases diagnosed as chronic cholecystitis and operated upon, no gallbladder disease was found in 22. There were five females to one male. X-ray diagnosis was correct in 95%. The mortality rate was 1.9%.

The authors stress the importance of adopting a more conservative approach to the treatment of acute cholecystitis because of the high mortality and morbidity associated with emergency surgery in this group. A palpable tender gallbladder is not a sufficient indication for emergency surgery. Perforated gallbladders will wall themselves off if left alone. The acute gallbladder should not be treated surgically without an adequate period of preparation, especially in the older age group, because of the seriously high mortality attending this type of emergency surgery. NORMAN S. SKINNER

Carcinoma of the Hepatic Flexure.

PHILLIPS, J. W., DOCKERTY, M. B. AND WAUGH, J. M.: CANCER, 8: 151, 1955.

Some hesitancy on the part of surgeons regarding the success of resection of carcinoma of the hepatic flexure is not justified. A review of 136 cases treated at the Mayo Clinic over 40 years showed that adverse findings, pathologically or surgically, were not commoner in carcinoma of the hepatic flexure than in tumours elsewhere in the colon. With the use of chemotherapy and modern support, there is no higher incidence of complications, and mortality rates and survival rates are similar. Fixation to adjacent structures is often inflammatory, so that

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attachment to the gallbladder, liver, or duodenum need not indicate inoperability. The five-year survival rate in this series was 56%. Without lymph node involvement the five-year survival rate was 79%, and fixation did not alter this, but if the fixation was neoplastic, the survival rate fell to 9%. BURNS PLEWES

OBSTETRICS

Phæochromocytoma and the Obstetrician.

GEMMELL, SIR ARTHUR A.: J. OBST. & GYNÆC. BRIT. EMP., 62: 195, 1955.

A phæochromocytoma is a localized tumour of the adrenal medulla which is functionally active in that it produces adrenaline and noradrenaline. Such tumours are sometimes bilateral and occasionally malignant. The symptoms associated with phæochromocytoma are often difficult to distinguish from those of eclampsia. We must, however, be aware of this tumour as a cause of such symptoms because its removal will cure the patient.

A pregnant patient with hypertension as a dominant physical sign may be suffering from toxæmia, essential hypertension or a phæochromocytoma.

It has been stated that in so-called malignant hypertension the proportion in which phæochromocytomas occur is about 5% or even higher. ROSS MITCHELL

The Effect of Hodgkin's Disease on Pregnancy and Fertility.

FRANK, H. G.: J. OBST. & GYNÆC. BRIT. EMP., 62: 266, 1955.

It is doubtful whether pregnancy has any effect on the course of Hodgkin's disease. There is, however, a risk that the patient's general condition may deteriorate during the course of the pregnancy unless precautions are taken. If the patient's condition is unsatisfactory and the disease becomes active, the prognosis may be poor because adequate treatment cannot be given.

The cause of lowered fertility in women suffering from Hodgkin's disease is not known, but may depend to a certain extent on factors not connected directly with the disease.

The advisability of marriage of patients suffering from Hodgkin's disease is discussed. ROSS MITCHELL

Lupus Erythematosus and Pregnancy.

TURNER, S. J., LEVINE, L. AND ROTHMAN, M. D.: AM. J. OBST. & GYNEC., 70: 102, 1955.

The available data disclosed a 20 to 60% maternal and 30 to 50% fetal mortality in acute and a 46% fetal mortality in subacute disseminated lupus erythematosus complicated by pregnancy.

Patients with any form of lupus erythematosus may tolerate pregnancy well, provided the disease is quiescent and under control. Interruption of pregnancy may have to be considered in cases where the disease cannot be controlled medically. The introduction of ACTH and cortisone as therapeutic agents may be of value in controlling the disease. More women may then live long enough to have uneventful pregnancies.

A plea is made for careful observation and reporting of lupus erythematosus complicated by pregnancy.
ROSS MITCHELL

Influence of Antibiotics on Pelvic Inflammatory Disease.

DEALVAREZ, R. R. AND FIGGE, D. C.: OBST. & GYNÆC., 5: 765, 1955.

Pelvic inflammatory disease should be initially treated conservatively; by so doing, the necessity for surgical management is reduced significantly.

More than 90% of patients with pelvic inflammatory disease will generally respond to conservative therapy. Bacteriological studies suggest that the etiological agents of this disease are varied. Evidence of specific origin is generally lacking. Conservative therapy should be continued until such time as it fails to result in permanent quiescence. When conservative therapy fails, surgery offers the only permanent means of cure, but surgical intervention is indicated in less than 10% of patients with pelvic inflammatory disease. ROSS MITCHELL

Maternal Factors that Influence the Severity of Erythroblastosis Fetalis.

TEATE, H. L. JR.: OBST. & GYNEC., 5: 819, 1955.

It is never justified to discourage further pregnancy for a sensitized mother regardless of maternal history or antibody titre, provided the mother is willing to take the risk of stillbirth. If the infant is liveborn, it has an excellent chance of survival and neurological normalcy if adequately and immediately treated. ROSS MITCHELL

PÆDIATRICS

Obesity in Childhood.

WOLFF, O. H.: QUART. J. MED., 24: 109, 1955.

The controversial literature pertaining to childhood obesity is reviewed and a study presented of 100 children attending in consecutive order the obesity clinic at the Children's Hospital, Birmingham. The birth weights of these children were found to be average; their height was significantly above average but not above the average for children of the professional class. The onset of puberty was about a year earlier than in non-obese children. Rapid weight reduction by dietary treatment resulted in a decrease in the expected growth in height.

The author concludes that the above-average height, and the early onset of puberty, in obese children are the result of a food intake above requirements. The relatively slight retardation of growth caused by rapid weight reduction is of no disadvantage since these children are above average in height and also the tendency to delay the onset of puberty will allow a longer period of growth.
NORMAN S. SKINNER

The Treatment of Primary Tuberculosis in Infancy.

MEYER, M., MIDDLEBROOK, G. AND ROBINSON, A.: J. PEDIAT., 46: 398, 1955.

Primary tuberculosis in children less than a year old has a poor immediate prognosis, and has a marked tendency to become progressive. The chief aim of treatment should be to prevent this spread, and particularly the development of miliary tuberculosis and tuberculous meningitis.

A positive tuberculin test in an infant is an unequivocal sign that active tuberculosis is present, regardless of the apparent physical condition, or normality of the chest roentgenogram. The authors urge routine tuberculin testing in infancy and early childhood, preferably with old tuberculin or PPD, less desirably with the Vollmer patch test.

The contacts, particularly elderly contacts, of every child with a positive reaction must be checked, and the child separated from the source of infection. If the infant is still tuberculin-negative, prompt vaccination with BCG is indicated.

For tuberculin-positive children, without x-ray evidence of disease, a course of isoniazid (INH) is prescribed, 8 mg. per kg. per day, for six months. Half this dosage is then given for at least three more months.

Vigorous treatment is indicated for infants with a positive tuberculin test and x-ray evidence of tuberculosis. Oral administration of INH is reinforced by intramuscular injection of streptomycin, which acts synergistically. The latter is given every three days for one month, the dose depending on the baby's weight.
I. J. PATTON

RADIOLOGY

A Comparison of Fetal and Infant Death Rates in the Progeny of Radiologists and Pathologists.

CROW, J. F.: AM. J. ROENTGENOL., 73: 467, 1955.

That the amount of radiation received by radiologists under usual conditions does not have any very great effect on fetal and infant death rates in their children is suggested by a questionnaire study reported in this article.

Data available from work on experimental animals had indicated that only a very small fraction of genetic effects of radiations would be expected to appear in the immediate offspring of exposed fathers and only a small proportion of the total genetic damage would be manifest as fetal and infant deaths. The present study was carried out in order to see whether any such effects could be found.

It was initiated in August 1951, when 1,027 questionnaires were mailed to radiologists and 1,036 to a control group of pathologists chosen from the Directory of Medical Specialists. Data from married males only were considered. In all, questionnaires from 530 pathologists and from 655 radiologists were examined and form the basis for the findings presented. Publication of the results was delayed until analysis of data from a similar and larger study being conducted by other investigators could be completed. Comparisons are drawn.

This investigation showed no statistically significant differences between the frequencies of stillbirths and miscarriages in the wives of radiologists (16.6%) and in a control group of pathologists' wives (15.9%). This result is in agreement with that of the other study. Infant mortality rates also were not significantly different.

The author draws attention to the fact that data on fetal deaths are subject to many errors. A small difference between the rates in the two professional groups might be due to causes other than radiation. Furthermore, the assessment of genetic effects is complicated by the fact that only a very small fraction of the total genetic damage would be detected as an increase in fetal and infant death rates in the first-generation progeny. The author therefore regards the negative results of this study as having little bearing on the question of genetic hazards from exposure to radiation. MARGARET H. WILTON

DERMATOLOGY

Cutaneous Manifestations of Myelogenous Leukæmia.

COSTELLO, M. J. ET AL.: A. M. A. ARCH. DERMAT., 71: 605, 1955.

The authors divide into two groups the types of cutaneous eruptions seen in myelogenous leukæmia. One group is the leukæmids or non-specific lesions, and the other is the true leukæmic infiltrations or specific lesions. The leukæmids most frequently seen are pruritus, urticaria, erythema multiforme-like lesions, petechiæ and hæmorrhages. Rarely, vesicular eruptions may occur. The urticaria lesions seen are less evanescent and more papular than the usual type of urticaria. More than one type of lesion may be present at one time. The most common specific skin lesions are tumours which rarely regress spontaneously or ulcerate. The trunk and external surfaces of the arms and legs are most often involved. In contradistinction to lymphatic leukæmia, the skin of the head is only rarely affected in myelogenous leukæmia. Erythroderma (generalized exfoliative dermatitis) is rarely associated with myelogenous leukæmia.

The authors point out the importance of looking for skin lesions, as they may precede by weeks, months, or occasionally years, the appearance of typical pathological changes elsewhere. Four cases of myelogenous leukæmia with cutaneous manifestations are presented in some detail. One case had ulcerating phlegmonous tumours, one had nodular and tumour-like non-ulcerating infiltrations, one had hæmorrhagic cutaneous blotches and hæmorrhagic bullæ, and one had macules, pruritic papules, papulovesicles, purpuric nodules and ulcerating tumours. ROBERT JACKSON

THERAPEUTICS

Convulsive Therapy in Psychoses Accompanying Pregnancy.

LAIRD, D. M.: NEW ENGLAND J. MED., 252: 934, 1955.

Electroconvulsive therapy was administered to eight mentally disturbed pregnant women, two receiving treatment during the final week of gestation, without untoward reaction in patient or offspring. This experience coincides with conclusions drawn from a review of the literature that electroconvulsive therapy may safely be employed in the presence of pregnancy. Insulin shock therapy would appear to carry a serious threat to the life of the fetus. NORMAN SKINNER

Possible Therapeutic Value of Cholecystectomy in Adams-Stokes Disease.

MCLEMORE, G. A., JR. AND LEVINE, S. A.: AM. J. MED. SC., 229: 386, 1955.

There has long been more than a suspicion that some relationship exists between the gallbladder and the heart. Transient auricular fibrillation, particularly, has been thought to have this mechanism in some instances. Furthermore, anginal pain in some patients has been thought to develop as a result of a trigger mechanism coming from a diseased gallbladder.

This report describes experiences with six patients with Adams-Stokes syndrome and one patient with complete heart block without syncopal attacks, who underwent cholecystectomy for incidental cholelithiasis. There was no operative mortality though three had attacks of asystole during anæsthesia. In each case, the incidence of attacks of syncope was decidedly decreased during the follow-up period; and in four cases the improvement was very striking. It would appear that the removal of a diseased gallbladder may not only relieve the patient of biliary symptoms, but also improve the cardiac status in selected cases of complete heart block with attacks of Adams-Stokes syncope. S. J. SHANE

Treatment of a Patient with Lupus Erythematosus and Pulmonary Tuberculosis with ACTH, Streptomycin and Para-aminosalicyclic Acid.

JOHNSON, J. R. AND DAVEY, W. N.: ANN. INT. MED., 42: 1,109, 1955.

Corticotropin (ACTH) and cortisone are regarded as contraindicated in the presence of tuberculosis because of their suppressive effect on inflammation, granulation tissue formation and fibroblastic repair. However, the administration of these drugs in human tuberculosis, covered by antimicrobial therapy, has not been shown to be harmful. In this report, a patient with far-advanced cavernous pulmonary tuberculosis was put on streptomycin and PAS in January 1952. ACTH therapy was started three weeks later, and continued for seven months, because of co-existing disseminated lupus erythematosus. Within eight weeks of the start of hormone therapy, the extensive bilateral exudative disease cleared remarkably, the cavity closed without collapse procedures, and the sputum cultures became negative. All symptoms cleared in the first few days of treatment, and sputum positivity declined steadily over several weeks. The writers consider this a further indication that antimicrobial therapy may prevent the adverse effects of

ACTH and cortisone on tuberculosis. They suggest cautiously that advantage might be taken of certain effects of these agents desirable in treating tuberculosis itself, by affording symptomatic relief in acute and desperate illness, and by inhibition of excess granulations and fibrosis. They point out that this therapeutic combination has been attempted with some degree of success in tuberculous meningitis. S. J. SHANE

INDUSTRIAL MEDICINE

Industrial Asthma and Bronchitis.

SCHEPERS, G. W. H.: INDUST. MED., 24: 53, 1955.

The author examines the concept of bronchitis or asthma as an occupational disease as evolved from recent investigations. He discusses in detail the available evidence that both asthma and bronchitis may result from exposure to certain occupational respiratory hazards, but emphasizes the fact that not every case in an industrial worker is necessarily due to work in such hazardous surroundings. Every case should be judged on its own merits. Before a favourable medico-legal determination can be made, investigation must be instituted and various critical diagnostic criteria satisfied. The significance of additional factors—allergy, infection, drugs, medicines, nutrition habits, and psychosomatic influences—must be considered, and also that of pre-existing or superimposed disease.

A wide variety of separate and unrelated industries have each yielded their quota of occupational asthmatics; many suffered also from bronchitis. One investigator has enumerated 38 responsible occupations; the employees covered had been exposed to no less than 144 effective incriminating agents. In all these cases, however, contributing factors were identified, including many which were themselves of occupational origin. Reference is made to byssinosis, bagassosis, asthma in handlers of cereals and other types of seeds, bronchial syndromes in brewers, haymakers and woodworkers, and allergies to hides, wool and down. The allergic or sensitizing factors are indicated.

Of the chemical substances used in industry, many are apparently inert as far as the bronchial system is concerned; others can promote acute and chronic respiratory disease. These include certain cadmium fumes, chromium, fluorides, osmium tetroxide, bromine, iodine or chlorine fumes; vanadium pentoxide, acetaldehyde and acetone. Consideration of the known effects of these and other chemical substances in common use indicates their significance when they become components of air pollution. Dust too has been incriminated.

The author points out that the above are mostly isolated occurrences in industrial medicine. Bronchitis and asthma acquire their real significance as causes of disability or death in their relation to asbestosis, anthracosis, siderosis and silicosis. He quotes extensively from investigations of the present century. A survey in the Union of South Africa established the fact that bronchitis was present in every case of silicosis subjected to autopsy. Other investigations have indicated the role of bronchial asthma in asbestosis. Bronchitis and bronchiectasis are essential components of the asbestotic phenomenon and it is in relation to the metaplastic and adenomatous states which ensue that the enhanced bronchial cancer rate may have its true significance. There is considerable divergence of opinion on anthracosis, but in the author's opinion there can be no doubt that under certain circumstances bronchitis and asthma do arise out of the coal-mining occupation. Various explanations are given.

Reference is made also to the role of bronchitis as a cause of death in the cutlery trade, and the improvement in health which has been achieved through the substitution of non-siliceous grinding tools. Observations in the miners of Schneeberg and Joachimsthal have established the fact that in those who do develop cancer, a bronchitis-like state preceded this occurrence by many years. The author considers it strongly possible that quartz is the cause. Tracheobronchitis has been noted as an early feature of beryllium exposure. Attention is drawn too to associated stress factors connected with mining, to radioactivity, to spores of the fungi which flourish on mine timber, and to atmospheric inclemencies. All these observations provide reason for further speculation concerning the nature of industrial bronchitis, and stress the urgent need for further epidemiological, pathological, anatomical and experimental research.

MARGARET H. WILTON

Chlorinated Insecticides: Toxicity for Man.

MCGEE, LEMUEL C.: INDUST. MED., 24: 101, 1955.

The accomplishments of insecticides—both in the control of zoological vectors and reservoirs of human disease, and in enabling the world to produce more food—have been widely acknowledged during the last decade. Their potential hazard to man must be recognized, but this must be clearly balanced against the gains in human lives protected from illness and death due to infectious disease and starvation.

Existing information is reviewed on toxicity to man of the chlorinated insecticides: chlorophenothane (DDT), benzene hexachloride, chlordan, aldrin, dieldrin, and toxaphene. This chlorinated hydrocarbon group are similar as regards: (a) solubility in fats and common organic solvents; insolubility in water; (b) relative chemical stability; (c) action as convulsant poisons in warm-blooded animals. Details are given regarding the rare reported cases of human poisoning due to accident or suicidal intent. In these instances the manifestations are sufficiently dramatic to make the diagnosis obvious, but the stress of the event frequently accounts for inaccurate reporting. Information on DDT is more extensive than that on the other insecticides. Acute poisoning, the effects on skin, the complication of other factors such as the solvent used and the possibility of chronic poisoning are all discussed. In the author's opinion, a statement first made in 1953 is correct: "There are no confirmed cases of chronic DDT poisoning, and confirmed cases of acute poisoning are invariably associated with the eating of a relatively large quantity of DDT."

Treatment of acute poisoning from chlorinated insecticides involves prompt removal of unabsorbed pesticide from the stomach or from the skin, and control of convulsions by adequate sedation (intravenous barbiturates).

Very recently (the summer of 1954) it became evident that human exposure to highly concentrated dusts can lead to clinically significant pulmonary and skin absorption of chlorinated insecticides. Workers were engaged in mixing, grinding and bagging 40% chlorinated insecticide dust. No masks were worn and the only ventilation was by air currents through doors and windows of a work shed. They worked on a schedule of eight hours on and eight hours off in continuous operation for a period of 88 hours. Fatigue and irritation of the eyes, followed on the fourth day by generalized convulsions in three of the men, resulted in all being sent to hospital for medical examination. Recovery was prompt and has not been followed by any characteristic sequelæ. In the author's opinion absorption of the chlorinated insecticides (pulmonary, cutaneous, and to some extent by the gastrointestinal tract) was the cause of the acute illness. This experience adds weight to the recommendations for limiting exposure of such workers by sensible operating practices.

The actual relationship, if any, of these materials to certain obscure diseases in man is unknown.

MARGARET H. WILTON

OBITUARIES

DR. WILLIAM A. DOBSON, for 36 years a physician and psychiatrist in Vancouver, died in that city on August 1 at the age of 70. Dr. Dobson was born in Tatamagouche, N.S., and taught school in Nova Scotia after graduating from Pictou Academy. After completing his medical course at Jefferson College, Philadelphia, he went to Vancouver, where he served his internship in the General Hospital. He later became interested in psychiatry, and was neurologist and psychiatrist at the General, Grace, and Crippled Children's Hospitals.

Dr. Dobson is survived by one brother.

DR. REAL DORE, 64, died in Montreal on August 22 after a long illness. He was born in Quebec, attended l'Ecole Normale de Québec, and graduated in medicine from Laval University in 1916. From 1917 to 1935 he was attached to Nôtre Dame Hospital, and afterwards to Verdun General Hospital. In 1926-27 Dr. Doré studied surgery in Paris. He was a consulting physician to Ste. Justine's Hospital, a member of the College of Physicians and Surgeons of the Province of Quebec, and a corresponding member of the American Goiter Association.

He is survived by his widow, two daughters, and four sons.

DR. PHILIP ERNEST DOYLE, a medical practitioner at Moose Creek, Ont., for the past 27 years, died on August 19, at the age of 70. Dr. Doyle was born at Hawkesbury, Ont., and graduated from McGill University in 1910. Before establishing practice at Moose Creek he was connected with the Royal Canadian Mounted Police and stationed in Herschel Island and Fort Churchill.

He is survived by his widow and one son, Dr. Philip J. Doyle of Peterborough.

DR. FREDERICK WILLIAM HARVEY, a pioneer in physiotherapy in Canada, died in the Montreal General Hospital on August 18. He was 83.

Dr. Harvey was born at Abbots Corner, Que., and studied medicine at McGill University, graduating in 1898. In 1904 he was appointed medical director of physical training in the university. He was largely instrumental in establishing, in 1908, the McGill School of Physical Education, which gave courses in physiotherapy for the first time in Canada. He also lectured in physiotherapy in the Faculty of Medicine and was clinical assistant in orthopædics at the Montreal General Hospital. During World War I he was medical officer of the McGill C.O.T.C. and physician in charge of physiotherapy at the Montreal Military and Montreal General hospitals. Later he was appointed director of the physiotherapy department of the Montreal General Hospital, a position which he held until his retirement a few years ago. He retired from McGill as university medical officer in 1938 but continued in his private practice until 1949, when he also relinquished his duties as medical examiner for the Metropolitan Life Insurance Company, with which he had been associated for 47 years. Until his death Dr. Harvey remained a member of the consulting staff of the Montreal General Hospital. He was a governor of the hospital.

He is survived by his widow, four daughters, and two sons, one of whom is Dr. R. F. Harvey of Montreal.

DR. CHARLES STAPLES HAWKINS, a physician in Toronto for nearly 50 years, died in that city on August 24. Dr. Hawkins was born at Canton, Ont., and graduated from the University of Toronto in 1906. He had been chief gynæcologist at the old Grace Hospital and was on the staff of the Toronto Western Hospital after the amalgamation of the two hospitals. Dr. Hawkins was one of the first occupants of the Medical Arts Building in Toronto. Since 1950 he had been living in retirement.

He is survived by his widow and two daughters.

DR. ROBERT ANDREW HICKS, a member of the staff of Colonel Belcher Hospital, Calgary, for the past nine years, died in that hospital on August 15 after a brief illness. He was 56.

Dr. Hicks was born in Lambton County, Ont., and moved to High River, Alta., with his parents in 1912. He graduated in medicine from the University of Alberta in 1928 and served from 1932 to 1936 on the staff of the Banff Mineral Springs Hospital. During World War II he served overseas for six years with the 8th Field Ambulance and on his return to Calgary in 1946 took over the command of the 8th Field Ambulance Reserve with the rank of lieutenant-colonel.

Surviving are his widow and one daughter.

DR. HEREWARD DAVIE LIVINGSTONE died at his home in Weston, Ont., on August 22. A specialist in diseases of the ear, nose and throat, he had retired from practice ten years ago.

Dr. Livingstone was born at Brussels, Ont., and was a great-nephew of Dr. David Livingstone, the noted explorer. After graduating in medicine from Trinity College, Toronto, he practised for 20 years in Rockwood, Ont. He then took postgraduate work at Manhattan Hospital, New York, before continuing his practice as a specialist in Toronto, in 1912.

He is survived by his widow.

DR. ANTHONY OSCAR TURNER, 67, died in Saskatoon on July 31. He was born in Durham, Ont., and took up residence in Invermay, Sask., in 1905. His medical education was interrupted by service overseas with the Medical Corps from 1915 to 1918. He practised medicine in Theodore, Sask., from 1920 until 1941, when he moved to Melville, and in Saskatoon from 1941 until his retirement in 1952.

Dr. Turner is survived by his widow, four sons and one daughter.

DR. HIRAM WRIGHT, a practising physician in Keene, Ont., for 20 years, died at his home on August 23 after a long illness. He was born at Cobden, Ont. After service with the Medical Corps in the First World War he practised medicine for a short time at Hanover and then at Churchill. In 1928 he went to Keene, where he was in practice for 20 years. In 1948 he joined the Federal Government's immigration department, examining prospective immigrants to Canada in England, Germany and Sweden. On his return to Canada in 1949 he was appointed medical officer for the Keene board of education, continuing in this office until his retirement in 1952.

Dr. Wright is survived by his widow, a son, and two daughters, one of whom is Dr. Lois Crawford of Vancouver.

LORD HORDER OF ASHFORD

We regret to announce the death on August 13 of Lord Horder, considered by many to be the leading British clinician of his time. He was also the best known doctor in the United Kingdom. In addition to a busy life in clinical medicine, including 25 years on the honorary staff of St. Bartholomew's Hospital, London, Lord Horder served the public in a great number of fields. He was an ardent advocate of cremation and of noise abatement, was active on the Empire Rheumatism Council and British Empire Cancer Campaign, and took a great interest in physical training and eugenics.

As medical adviser to royalty and leading politicians, including Sir Winston Churchill, he was much in the public eye. As an outspoken opponent of the State monopoly in medicine in the United Kingdom, he attracted much attention within the profession in recent years. He leaves behind the memory of a man who had lived to the full every minute of the 84 years allotted to him.

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NEWS ITEMS

SASKATCHEWAN

The arrival of Saskatchewan's first professor of pædiatrics has been announced by the University in Saskatoon. Dr. John W. Gerrard, B.A., B.Ch., D.M.(Oxon.), M.R.C.P.(London), came from England in July to take up his new teaching post and to organize the department of pædiatrics at the University Hospital. Born in Northern Rhodesia, Professor Gerrard took his B.A. in Physiology at Oriel College, Oxford, and did his clinical studies at Birmingham, graduating in 1941. He served first with a field ambulance in North Africa and then with the first reconnaissance regiment of the First British Army. He was with this unit at the Anzio landings in Italy. In 1945 he became Deputy Assistant Director of Medical Services for the First Division with headquarters in Palestine. After the war Professor Gerrard returned to Birmingham to resume the study of children's diseases under the late Sir Leonard Parsons. In 1948 he became lecturer in pædiatrics and in 1951 was appointed chief assistant to Professor Smellie and consultant pædiatrician at the Children's Hospital, Birmingham. Last year he spent several months at Johns Hopkins Hospital and visited a number of North American centres. His research and publications are chiefly concerned with kernicterus, hæmolytic disease of the newborn, cœliac disease and phenylketonuria.

A pleasing increase in student participation in research at the College of Medicine is announced by Dean J. W. Macleod. By means of the Lederle Research Fellowship and grants from the Dr. Peter Donald Stewart Bequest to the University of Saskatchewan, it has been possible for six students to spend the summer vacation working with their teachers in the Departments of Anatomy, Bacteriology, Physiology and Surgery. E. Nykiforuk is working with Dr. Wolfgang Fritsche on the fibre architecture of the deep fascia of human arms and legs. Philip Adilman is associated with Mr. Alex Bakerspigel in a study of the fungi of the rodents in Saskatchewan with particular attention to Endogone. Fred Morris, who is entering fourth year at the University of Manitoba, is continuing his study of the effects of heparin on the adrenohypophyseal system with particular reference to blood glucose and pyruvic acid (with Dr. L. Hamilton) and the liver enzyme, tryptophane peroxidase (with Dr. J. Lowenthal). R. O'Toole is continuing with Professor L. B. Jaques his study of the action of dicoumarol using radioactive tracers, which he began as a student in physiology for his Master's degree. Peter Siemens is assisting Dr. John Merriman in an experimental study of the influence of bronchial artery occlusion on individual lung function. Robert Cooper is working with Professor Nanson on the production and repair of interatrial septal defects in the dog. He is also trying to learn more about the influence of electrolytes on heart action during dog surgery.

Participation by the student in scientific research need not deflect him from the goal of practising good medicine at the bedside or in the small hospital, the dean insists: it promotes an attitude of open-minded inquiry and critical appraisal of phenomena—qualities to be sought in any role in medicine. The university seeks further funds to permit students to spend their vacation in this profitable manner.

Dr. S. E. Moore, one of Regina's senior medical practitioners, was honoured during July at a dinner given by the Regina General Hospital Board in the hospital cafeteria. After 45 years of continuous service Dr. Moore is retiring as a lecturer in surgery to the hospital's School of Nursing. He will, however, continue his private practice.

Dr. Gordan Grant, Chairman of the Board, presented Dr. Moore with a scroll of honour stating, "Dr. Moore has devoted 45 years to his profession, and has made a success of it. He has been a champion of the general practitioner in this day of specialists, and one of the highlights of his career was his contribution toward the founding of the Royal College of Surgeons of Canada."

Tuberculosis sanatoria of Saskatchewan had higher operating costs in 1954 than in 1953, but there was a compensating slight drop in the number of patient-days. Forty-two deaths from tuberculosis were reported, 30 in whites and 12 in Indians. This is a rate of 4.8 per 100,000 population. G. W. PEACOCK

ONTARIO

The Workmen's Compensation Board is to build a modern rehabilitation centre on a 65-acre site at Wilson Avenue, 13 miles from downtown Toronto. This new 500-bed building will replace the temporary quarters at Malton.

The recently appointed advisory committee to the provincial government on rehabilitation includes E. A. Baker, managing director of the Canadian National Institute for the Blind; John C. Counsell, president and managing director, Canadian Paraplegic Association; R. W. Hopper, executive director of the Crippled Children's Society; Edward Dunlop, executive director of the Canadian Arthritis and Rheumatism Society; and Dr. Glenn Sawyer, secretary of the Ontario Medical Association.

A 560-bed treatment unit for tuberculosis patients, costing about $2,400,000, is to be built at the Ontario Hospital, Woodstock. This is the centre for treating tuberculosis patients from provincial mental hospitals.

In the first formal graduation held in the course, 16 young women representing six city hospitals were graduated as registered technologists at a ceremony in Sunnybrook Hospital, Toronto. The 12-month course is a certified examination course under the Canadian Medical Association. It covers all phases of laboratory work.

The following staff changes in the Faculty of Medicine, University of Toronto, have been announced: Dr. M. H. Brown, professor of hygiene and preventive medicine, is to head the department. Dr. K. W. G. Brown is to be the first Rykert research cardiologist for 1955-56.

Promoted to the rank of associate professor are Dr. W. G. B. Castleman of the Banting and Best Department of Medical Research; Drs. D. N. Henderson and H. W. Johnston in Obstetrics and Gynæcology; Drs. F. C. Monkhouse and A. M. Rappaport in Physiology; Dr. J. W. L. Doust in Psychiatry and Dr. W. G. Bigelow in Surgery.

Promoted to the rank of assistant professor are: Drs. C. R. Burton, C. C. Gray, W. F. Greenwood, W. E. Hall, D. B. Moran, M. A. Ogryzlo and W. A. Oille in medicine; Drs. J. Mann and G. L. Watt in Obstetrics and Gynæcology; Drs. W. G. Carscadden, J. L. T. Russell, C. M. Spooner, C. H. Watson and A. W. M. White in Surgery.

The following awards have been granted to graduates from the Faculty of Medicine, University of Toronto: Graham Campbell Fellowship, Dr. H. J. Watt; William Goldie Prize, Dr. R. L. MacMillan; Percy Hermant Fellowships in Ophthalmology, Drs. D. W. Harper, R. D. Lawton and M. Neveu; Arch Hutchinson Fellowship, Dr. K. R. Butler; Minister of Health Gold Medal in Psychiatry from the Province of Ontario, Dr. P. A. Christie; Alexander McPhedran Research Fellowship in Clinical Medicine, Dr. G. W. Fitzgerald; O'Keefe Fellowship in Oto-Laryngology, Dr. T. Molony; Starr Medal, Dr. S. J. Klebanoff; Helen L. Vanderveer Fellowship, Dr. H. J. Watt.

Awards to undergraduates in the fourth medical year were: Cody Gold Medal, Mrs. M. L. Cohen; Cody Silver Medal, G. S. Cohen; Cody Silver Medal, R. M. Ehrlich; Dr. Benjamin W. Appleton Prize in Psychiatry, A. Piotrowski; Butterworth Prize, C. D. Anderson; Chappell Prize in Clinical Surgery, J. D. T. Ainslie; Hendry Memorial Scholarship, Mrs. J. S. Bain; Medical Alumni Association Scholarship, R. M. Ehrlich; Ellen Mickle Fellowship, Mrs. M. L. Cohen; Ontario Medical Association Prize in Preventive Medicine, G. S. Cohen; Doctor Roy Simpson Scholarship in Pædiatrics divided equally between J. D. T. Ainslie and R. M. Ehrlich.

LILLIAN A. CHASE

NOVA SCOTIA

Dr. David E. MacLeod, an R.C.A.F. officer formerly of Brule, Colchester County, who braved flames and danger of explosion in trying to save the lives of two officers of a burning jet fighter at North Bay last September, has been awarded the Queen's Commendation for Brave Conduct. F./L. MacLeod was on duty at the time of the accident, and within minutes after the crash was on board the burning aircraft trying to determine whether or not the occupants were alive. He did not leave until certain that both officers were already dead.

Dr. William Feindel has been appointed associate professor of surgery in the College of Medicine at the University of Saskatchewan, and director of the division of neurosurgery at the University hospital. He is a graduate in Arts of Acadia, where he won a Rhodes Scholarship to Oxford in 1939. During his student days at McGill he was research assistant at the Montreal Neurological Institute under Dr. Wilder Penfield.

The marriage of Dr. Franklyn H. Hicks of Halifax and Bridgetown, N.S., to the only daughter of the Bishop of Upper Austria, the Right Reverend Wilhelm Mensing-Braum, and Mrs. Wilhelm Mensing-Braum of Linz, took place this summer in Einz-on-the-Danube, Austria.

The impressive ceremony performed by the bride's father was witnessed by a host of friends from Austria, Germany, England, Canada, France and Italy. Guests from Canada included the Hon. Henry O. Hicks, Premier of Nova Scotia, Dr. N. S. Black, Amherst, and Dr. H. W. Soby of High River, Alberta.

Dr. S. W. Williamson recently celebrated his 86th birthday. He still enjoys outdoor skating, and is Yarmouth's oldest doctor as well as being coroner for that county.

Dr. D. Lawrence Sutherland, of Pictou, has completed a series of postgraduate studies and has announced the opening of an office in Windsor, Ontario, for the practice of neurological surgery. He did postgraduate work at Massachusetts General and Albany Hospitals as well as at the Montreal Neurological Centre.

Dr. C. L. Gass, now living in Tatamagouche, was one of four Maritimers honoured by Mount Allison with an honorary LL.D. degree at the spring convocation. He formerly practised in Sackville, N.B.

Dr. J. A. Glorioso was recently installed as chief of staff at St. Rita's Hospital, Sydney. For a number of years he was engaged in private practice in Lima, Ohio.

C. M. HARLOW

FORTHCOMING MEETINGS

CANADA

SOCIETY OF OBSTETRICIANS AND GYNÆCOLOGISTS OF CANADA—1956 Annual Meeting, Manoir Richelieu, Murray Bay, Quebec. (Dr. F. P. McInnis, Secretary, Society of Obstetricians and Gynæcologists of Canada, 1230 Avenue Road, Toronto, Ont.) June 8-10, 1956.

CANADIAN SOCIETY FOR THE STUDY OF FERTILITY, Royal York Hotel, Toronto, Ont. (Dr. Earl R. Plunkett, Secretary Treasurer, Canadian Society for the Study of Fertility, 469 Waterloo Street, London, Ont.) October 6-8, 1955.

UNITED STATES

ANNUAL ASSEMBLY IN OTOLARYNGOLOGY, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12, Illinois. (Dr. F. L. Lederer, Professor and Head of the Department.) September 19-October 1, 1955.

AMERICAN MEDICAL WRITERS' ASSOCIATION, 12th Annual Meeting, Hotel Jefferson, St. Louis, Missouri. (Dr. H. Swanberg, Secretary, 209-224 W.C.U. Bldg., Quincy, Ill.) September 30, 1955; Workshop, October 1, 1955.

MIDWEST CONFERENCE ON RHEUMATIC DISEASES, Henry Ford Hospital, Detroit, Michigan. (Dr. J. Lightbody, Medical Director, Michigan Chapter, Arthritis & Rheumatism Foundation, 7338 Woodward Avenue, Detroit 2, Michigan.) October 5, 1955.

AMERICAN ACADEMY FOR CEREBRAL PALSY, ANNUAL MEETING, Memphis, Tennessee. (Dr. R. A. Knight, Secretary-Treasurer, 869 Madison Avenue, Memphis 3, Tenn.) October 10-12, 1955.

AMERICAN HEART ASSOCIATION, Annual Meeting and Twenty-Eighth Annual Scientific Session, Jung Hotel, New Orleans, Louisiana. (The Medical Director, American Heart Association, 44 East 23rd Street, New York 10, N.Y.) October 22-26, 1955.

INTERNATIONAL ANÆSTHESIA RESEARCH SOCIETY CONGRESS, Washington, D.C. (Dr. William Friend, 515 Nome Avenue, Akron, Ohio.) October 24-27, 1955.

INTER-SOCIETY CYTOLOGY COUNCIL, 3rd Annual Meeting, Statler Hotel, Cleveland, Ohio. (Dr. P. F. Fletcher, Secretary-Treasurer, 634 N. Grand Blvd., St. Louis 3, Mo.) November 11-12, 1955.

AMERICAN PUBLIC HEALTH ASSOCIATION, INC., 83rd Annual Meeting and Meetings of Related Organizations, Kansas City, Missouri. (The American Public Health Association, Inc., 1790 Broadway, New York 19, N.Y.) November 14-18, 1955.

NATIONAL SOCIETY FOR CRIPPLED CHILDREN AND ADULTS, Annual Convention, Palmer House, Chicago. (Director of Information, 11 South LaSalle Street, Chicago 3, Illinois.) November 28-30, 1955.

AMERICAN MEDICAL ASSOCIATION, Clinical Meeting, Boston, Massachusetts. (Dr. George F. Lull, 535 North Dearborn Street, Chicago 10, Illinois.) November 29-December 2, 1955.

AMERICAN PSYCHOSOMATIC SOCIETY, 13th Annual Meeting, Sheraton Plaza Hotel, Boston. (Dr. S. Cobb, Chairman, Programme Committee, 551 Madison Avenue, New York 22, N.Y.) March 24-25, 1956.

OTHER COUNTRIES

COUNCIL FOR INTERNATIONAL ORGANIZATION OF MEDICAL SCIENCES, THIRD GENERAL ASSEMBLY, Paris, France. (C.I.O.M.S., 19 Avenue Kléber, Paris 16, France.) September 30, October 1, 1955.

ASSOCIATION OF CLINICAL PATHOLOGISTS — GENERAL MEETING, Royal College of Surgeons, London, England. (Dr. W. H. McMenemy, Maida Vale Hospital for Nervous Diseases, London, W. 9, England.) September 29-30, October 1, 1955.

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ASSOCIATION OF CLINICAL BIOCHEMISTS AND ASSOCIATION OF CLINICAL PATHOLOGISTS—JOINT MEETING, London, England. (Dr. H. Lehmann, Department of Pathology, St. Bartholomew's Hospital, London, E.C. 1, England.) October 1, 1955.

FIRST INTERNATIONAL CONGRESS OF MEDICAL ETHICS (Premier Congrès International de Juridiction Professionnelle Médicale et de Droit Médical Comparé), Paris. (Congress Secretary: Conseil National de l'Ordre des Médecins, 60 Boulevard Latour-Maubourg, Paris 7e). September 30, October 1-3, 1955.

14TH FRENCH STOMATOLOGY CONGRESS, Paris, France. (Dr. Robert Vrasse, Stomatologiste des Hôpitaux, 2 rue de Miromesnil, Paris 8, France.) October 3-9, 1955.

BRITISH ORTHOPÆDIC ASSOCIATION—Annual Meeting, Liverpool, England. (The Association, 45 Lincoln's Inn Fields, London, W.C.2, England.) October 6-8, 1955.

INTERNATIONAL ACADEMY OF LEGAL MEDICINE AND SOCIAL MEDICINE, FOURTH INTERNATIONAL CONGRESS, Genoa, Italy. (Professor P. Dervillée, 159 rue de la Croix de Seguey, Bordeaux, France.) October 13-17, 1955.

NUTRITION SOCIETY—Symposium, London, England. (Dr. R. J. L. Allen, Monkhouse and Glasscock Ltd., London, S.E.1, England.) October 15, 1955.

CONGRESS OF THE INTERNATIONAL UNION OF THE MEDICAL PRESS, Paris, France. (Jean Mignon, Secretary-General, "Le Concours Médical," 37 rue de Bellefond, Paris 9e.) October 16-20, 1955.

MEDICAL ASSOCIATION OF SOUTH AFRICA—40th Medical Congress, Pretoria, South Africa. (Joint Organizing Secretaries, Room 28, Administrative Building, General Hospital, Pretoria, South Africa.) October 17-22, 1955.

PAN-AMERICAN CONGRESS, International Congress of Surgeons (in conjunction with Argentine conference on thoracic surgery), Mendoza, Argentina. (Biblioteca, Asociacion Medica Argentina, Santa Fé 1171, Buenos Aires, Argentina.) October 22-26, 1955.

INTERNATIONAL PLANNED PARENTHOOD FEDERATION—Fifth Conference, Tokyo, Japan. (Mr. Juitsu Kitaoka, c/o S. Kato, Sangiin Kaikan, Chiyoda-ku, Tokyo, Japan.) October 24-29, 1955.

ASSOCIATION OF ANÆSTHETISTS OF GREAT BRITAIN AND IRELAND—Annual Meeting, London, England. (Association of Anæsthetists of Great Britain and Ireland, 45 Lincoln's Inn Fields, London, W.C.2, England.) November 3, 1955.

PHYSIOLOGICAL SOCIETY—Meeting, London, England. (Professor A. A. Harper, Dept. of Physiology, King's College, Newcastle-upon-Tyne, England.) November 4-5, 1955.

INTERNATIONAL CONGRESS OF ALLERGOLOGY, Rio de Janeiro, (Dr. F. W. Wittich, 424 LaSalle Medical Bldg., Minneapolis, Minn.) November 6-12, 1955.

SOCIETY OF THORACIC SURGEONS OF GREAT BRITAIN AND IRELAND, Glasgow, Scotland. (Mr. J. Leigh Collis, F.R.C.S., 15 Highfield Road, Edgbaston, Birmingham, England.) November 11-12, 1955.

SIXTH VENEZUELAN CONGRESS OF MEDICAL SCIENCES, Caracas, Venezuela. (Dr. A. L. Briceno Rossi, Apartado 4412, Ofic. del Este, Caracas, Venezuela.) November 18-26, 1955.

BRITISH ASSOCIATION OF SPORT AND MEDICINE—Meeting, St. Thomas's Hospital, S.E.1, London, England. (Dr. D. J. Cussen, British Association of Sport and Medicine, 95 Mount Street, London, W.1, England.) November 21, 1955.

INTERNATIONAL FERTILITY ASSOCIATION, SECOND WORLD CONGRESS, Naples, Italy. (Prof. G. Tesauro, President of Committee Arrangements, S. Andrea delle Dame, 19, Naples.) May, 1956.

BOOK REVIEWS

CARDIOLOGY NOTEBOOK FOR PRELIMINARY INSTRUCTION IN MEDICAL CURRICULA

A. P. Fishman et al., Columbia University College of Physicians and Surgeons, New York. 95 pp. Illust. $2.50. Grune & Stratton, Inc., New York and London, 1955.

The editors have designed this notebook for the medical student to bridge the gap between the basic sciences and clinical medicine in the field of cardiology. It is divided into four sections: cardiac fluoroscopy and radiography, electrocardiography, hæmodynamics and nomenclature for cardiac diagnosis. A brief description of the method of fluoroscopy is followed by a series of diagrams and pictures of heart models and radiographs illustrating various normal and abnormal states. A number of electrocardiograms showing various common abnormalities are then analysed. A particularly useful section presents the normal range of values for intracardiac pressures and blood gas analyses as well as the related data on pulmonary function. A brief outline of the nomenclature used by the New York Heart Association forms the fourth section. This should be a very useful summary for the medical student and intern.

CLUES IN THE DIAGNOSIS AND TREATMENT OF HEART DISEASE.

P. D. White, Consultant in Medicine, Massachusetts General Hospital, Boston. 186 pp. Illust. $6.00. Charles C Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1955.

This monograph by the distinguished Boston cardiologist, Paul White, consists of an informal discussion on various points about diagnosis and treatment, many of which are not to be found in the standard texts or in journals, and which usually come only as the result of experience. It includes not only the distillate of his own experience but also that of many cardiologists throughout the world. He discusses clues which may come from an intelligent inspection of the patient and from adroit probing of the past history and family history. The various symptoms of heart disease are analysed, particularly with respect to the possibility that they may be due to causes other than heart disease. The importance of a correct evaluation of physical signs is emphasized. Radiological and electrocardiographic studies are put in their proper perspective. A valuable but all-too-short chapter on therapeutics completes this valuable little book. It can be unreservedly recommended to both general practitioners and internists.

UNTERSUCHUNG UND BEURTEILUNG DES HERZKRANKEN (Examination and Assessment of the Cardiac Patient).

H. W. Knipping, Director, The Medical University-Clinic; W. Bolt, Chief Physician, The Medical University-Clinic; H. Valentin and H. Venrath, Assistants at The Medical University-Clinic, Cologne. 461 pp. Illust. 79 marks, paperbound; 83 marks, clothbound. Ferdinand Enke, Stuttgart, 1955.

This book deals with modern diagnostic methods in heart diseases with emphasis on special examinations necessary for the assessment of patients for cardiac surgery.

Normal and pathological physiology of heart and circulation, and the conventional diagnostic methods (physical examination, radiology and electrocardiography) are described briefly. Cardio-pulmonary function tests are dis-

cussed in detail, especially Knipping's ergospirometry. Cardiac catheterization, angiocardiography and selective angiography of the pulmonary vessels are also described and well illustrated. In the chapter on special preoperative diagnosis, the congenital malformations, valvular diseases, and coronary diseases are discussed in detail. There is also a special chapter devoted to a discussion of cor pulmonale. Special problems of anæsthesia and resuscitation during cardiac surgery are described.

The book should be of value to the German-reading practitioner and specialist in this field.

POLYPEPTIDES WHICH STIMULATE PLAIN MUSCLE.

Edited by J. H. Gaddum, Professor of Pharmacology and Materia Medica, University of Edinburgh, Scotland. 140 pp. $2.50. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1955.

Pharmacologists and physiologists have a penchant for treating and/or extracting various tissues and tissue fluids and testing the ability of these extracts to stimulate smooth muscle. Often this seems to be done out of curiosity and without any desire to find some substance to perform a known physiological role. Many of the substances, chiefly polypeptides, discussed in this symposium fall into this category (kallidin, substance P, bradykinin, substance U, substance Z, pepsanurin, pepsitocin and pepsitensin.) With regard to these, the main question which the average medical scientist wishes answered is whether they play any physiological role or whether they are interesting artefacts. The medical practitioner desires to know whether they have any clinical usefulness.

In other cases, substances have been looked for which could fulfil a role in some physiological or pathological process (vasopressin, oxytocin, angiotonin or hypertensin, cholecystokinin, VDM, VEM) or to explain an experimental result (Darmstoff). Here the chief question for the medical scientist is whether or not these substances can perform the roles for which they are candidates and whether they actually do.

If information is available to answer these questions and if this information has not been better dealt with elsewhere, this symposium might be of general medical interest. However, such information, as is apparent from the 15 contributions, is usually not available. Most of these substances have not even been purified (only oxytocin, vasopressin, VDM and possibly substance P) and the structure of substance P is still unknown. In those cases in which the possible physiological roles have been most carefully studied (oxytocin, vasopressin, VDM and VEM, angiotonin) the experiments have been dealt with extensively in other places. However, the contributions of H. B. Van Dyke on the posterior pituitary substance, I. H. Page on angiotonin, and E. Shorr on VDM and VEM are useful summaries.

This volume therefore is chiefly of interest to those who want a concise summary of available information on new polypeptides stimulating smooth muscle. In clearing up some confusion as to which substances are different in reality or in name only, this volume is of great value. The concluding discussion by Dr. Gaddum, the editor, is particularly helpful in this regard. Dr. Gaddum's opening remarks also contain valuable material outlining the methods by which various substances which stimulate smooth muscle may be differentiated; this should aid in clearing up remaining uncertainties about the identity of various compounds (e.g. bradykinin and kallidin). Dr. Gaddum also admirably explains the pitfalls in the overeager assumption that these materials may play a physiological role, and he lays down the steps through which a role may be established at some future date, for the remainder of these compounds.

For those interested in research dealing with these or related substances, this book provides a valuable summary and guide to the literature. However, the book contains none of the interchange of criticism, ideas and speculations which probably went on at the actual symposium and which might have been very helpful to those interested in these compounds. This is the result of the fact that papers were considerably revised for publication, and bear little relation to what was said at the symposium.

PRESERVATION AND TRANSPLANTATION OF NORMAL TISSUES

A Ciba Foundation Symposium.
G. E. W. Wolstenholme and M. P. Cameron, Editors for the Ciba Foundation, assisted by J. Etherington. 236 pp. Illust. $4.25. J. & A. Churchill Ltd., London, W. 1, England; British Book Service (Canada) Limited, Toronto, 1954.

This compact, well-produced and easily read book reports fully on the symposium attended by leading workers in a number of specialized fields related to the preservation and transplantation of tissues. The papers, varying from biophysics, physiology and tissue cultures, to surgery, ophthalmology and blood transfusions, are written clearly and the relevant references are given; in the discussion following each article interesting points are elaborated. The symposium was evidently a success and in all probability the contributors returned to their laboratories stimulated by new trends of thought.

Yet it is difficult to say who will be helped by this book. Those who are actively engaged on the work described here will know most of the information or be able to acquire it more adequately from standard reference works or review articles. To others the detailed experimental material will be too technical to evaluate properly. Dr. Earle's account of the evolution of large-scale tissue cultures is an example; it gives clearly the progressive steps in the procedures developed to grow L strain fibroblasts via cellophane and plain glass substrates to fluid suspension cultures. In this case the original papers will already have been read by tissue culture workers and to most others the material will be merely of superficial interest.

This book, therefore, does its job well but the actual value of that job is perhaps questionable. Nobody will question the merit of encouraging groups of allied scientists to meet together, but the benefit of these conferences is derived more from informal conversations than on-the-floor statements, and only the latter are available for reporting.

SURGERY OF THE CÆCUM AND COLON

S. Aylett, Surgeon, The Westminster Hospital Teaching Group (Gordon Hospital), The Metropolitan Hospital, Potters Bar and District Hospital; Teacher in Surgery, The University of London. 295 pp. Illust. $7.65. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Ltd., Toronto, 1954.

Undoubtedly the general arrangement of this book is excellent, the print is large and clear and many of the important points are given in larger type. The illustrations, too, are excellent. Certain sections of the book, such as those on the diagnosis of cancer of the colon, are rewarding. The reviewer agrees with the author when he states that there is not yet enough evidence to prove whether an end-to-end anastomosis or an abdominoperineal resection is the better operation for carcinoma.

When, however, he deals with ulcerative colitis his views would seem to be at variance with almost every one of the leading surgeons in this field. in the U.S.A. and in Canada. He scarcely mentions the early work

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done on this disease in this country and the U.S.A. His suggestion that an anæsthetic may be given in order to pass a sigmoidoscope seems unnecessary, as this has been done on innumerable occasions without pain or trouble. His statement that the improvement following the formation of an ileostomy is usually dramatic would seem to be an exaggeration, although the occasional mild case may benefit. However, the opinion with which most surgeons would quarrel most violently is his advocacy of the anastomosis of the ileum to the rectum following colectomy. Such a procedure has certainly not been successful in the vast majority of cases which the reviewer has seen or in those described in the various articles which have been published. It has been generally found, both in the U.S.A. and Canada, that if the ulcerative colitis is so severe as to require a colectomy, it is almost always impossible to restore the continuity of the bowel, and in fact it has been advocated by some that the terminal segment should be excised shortly after wards.

The author describes 30 cases successfully performed at the Gordon Hospital, London. One can only conclude that either: (1) the rectum was not involved in the first place; (2) the patients have not had a long enough follow-up, or (3) the English variety of this disease is quite different from that which we see on this continent.

This would seem to be misleading information, dangerous both to the patient and to the surgeon. Most surgeons in this country feel that patients should be warned that if a colectomy is necessary, they should be prepared to accept a colostomy for the remainder of their lives.

THE THERAPY OF SKIN TUBERCULOSIS.

G. Riehl, Professor of Dermatology, University of Vienna; Director, Lupus Institute of Vienna, and O. Köpf, Former Assistant, Lupus Institute of Vienna, Austria. Translated and revised by E. A. Strakosch, Director, Department of Dermatology, Presbyterian Hospital, Denver, Colorado. 247 pp. Illust. $7.50. Charles C Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1955.

This textbook covers a segment of dermatology not hitherto available to physicians interested in this problem. The presentation is precise, complete, and for the most part very practical. The dosage schedules and the drugs outlined in this book are for the most part readily available in this country.

The references included should prove most helpful to anyone doing work in this field; this must be one of the most complete bibliographies in English.

This book was favourably commented on by Dr. Henry E. Michelson of Minneapolis, who discussed it during the American Academy of Dermatology and Syphilology meeting held in Chicago last December.

THE LUNG. Clinical Physiology and Pulmonary Function Tests (Based on the 1954 Beaumont Lecture).

J. H. Comroe, Jr., Professor of Physiology and Pharmacology; R. E. Forster, II, Associate Professor of Physiology; A. B. Dubois, Assistant Professor of Physiology; W. A. Briscoe, Associate in Physiology; E. Carlsen, Isaac Ott Fellow in Physiology—all at the Graduate School of Medicine, University of Pennsylvania. 219 pp. $5.50. The Year Book Publishers, Inc., Chicago, Illinois; Burns & MacEachern, Toronto, 1955.

In the preface the authors state that the book was written for doctors and medical students, and not for pulmonary physiologists. The purpose of the book is to explain in simple words and diagrams those aspects of pulmonary physiology which are important to clinical medicine. The five authors have collaborated in producing an authoritative book on experimental and clinical procedures in relation to pulmonary function. This present work was prepared as an explanation of physiological principles rather than detailed procedures.

The first 141 pages are divided into seven chapters dealing with lung volumes, pulmonary ventilation, pulmonary circulation, diffusion of gases, arterial gases and pH and the mechanics of breathing. The second part of the book consists of 30 pages given to clinical applications of pulmonary function tests. The last part (appendix) consists of 42 pages of useful data, equations, calculations, and selected references. There are 58 exceedingly helpful figures and a very useful index.

The book will be most useful to the clinician specializing in diseases of the chest, to the enterprising anæsthetist, and most of all to the teacher of respiratory physiology. The advanced medical student will find in it much more than he requires for examinations, but no less than he may wish to know, or should know, about specific important details.

ELECTROCHEMISTRY IN BIOLOGY AND MEDICINE

Edited by T. Shedlovsky, Rockefeller Institute for Medical Research, New York. Sponsored by The Electrochemical Society, Inc., New York, N.Y. 369 pp. Illust. $10.50. John Wiley & Sons, Inc., New York, 1955.

This is a collection of 19 papers originally read at a Symposium on Electrochemistry in Biology and Medicine held in New York in April 1953. There is some coherence between the topics in the first half of the articles which deal with membrane transport and related bioelectric phenomena, but the rest of the papers are devoted to such diverse questions as, for example, the hydrogen ion titration curves of proteins, the polarographic behaviour of plasma protein fractions, and the preoperative EEG localization of brain tumours. The authors of the articles are experts in their fields, and the papers can be recommended as reviews of the more recent standpoints obtained in their respective specialties. The great variety of subject matter makes it desirable to have the individual articles catalogued instead of lumping them together under the general title "electrochemistry."

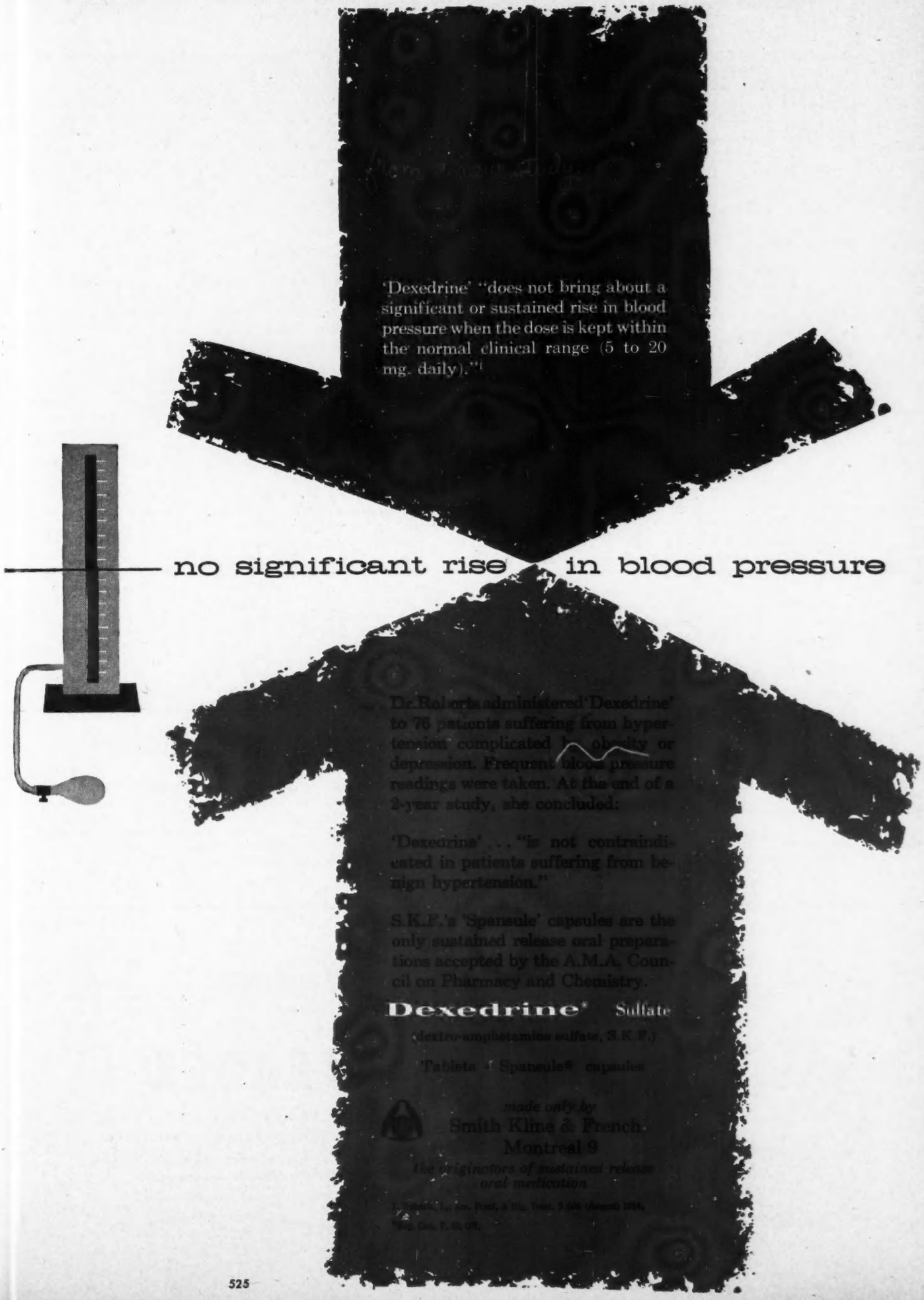
CLINICAL BACTERIOLOGY

E. J. Stokes, Clinical Bacteriologist, University College Hospital, London, England. 288 pp. $3.40. Edward Arnold (Publishers) Ltd., London, England; The Macmillan Company of Canada Limited, Toronto, 1955.

There are a number of excellent textbooks on bacteriology, giving detailed descriptions of micro-organisms, but most of these leave a gap between the patient ill with an infection and the identification of the causative organisms in the laboratory. It is in this field that Dr. Stokes's book is most valuable, and her approach to clinical bacteriology is a sound one.

The short introductory chapter on the interpretation of results is particularly good and the principles stated there can be profitably considered by the clinician as well as the clinical bacteriologist.

The techniques recommended differ in certain respects from those generally used in this country, but this should not be viewed as a criticism, as there are few other subjects where techniques vary as much as they do in bacteriology. The greater part of the book is devoted to a procedure to be followed in the treatment of specimens, and the isolation and identification of organisms, due space being given to antibiotic testing and serological techniques. The section on media preparation is of less


'Dexedrine' "does not bring about a significant or sustained rise in blood pressure when the dose is kept within the normal clinical range (5 to 20 mg. daily)."[1]
no significant rise in blood pressure
Dr. Roberts administered 'Dexedrine' to 76 patients suffering from hypertension complicated by obesity or depression. Frequent blood pressure readings were taken. At the end of a 2-year study, she concluded:
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interest to us, as many of the media used on this continent are prepared from dehydrated formulæ.

A chapter on hospital wound infections is one of interest to everyone concerned with such infections.

The book, with its very modest price, is a valuable one to the clinical pathologist and bacteriologist.

ACTA PSYCHIATRICA ET NEUROLOGICA SCANDINAVICA SUPPLEMENTUM 99: INDUCED ABORTION ON PSYCHIATRIC GROUNDS. (A Follow-up Study of 479 Women.)

M. Ekblad. From the Department of Psychiatry, Karolinska Institutet Medical School, University of Stockholm, Sweden. 237 pp. Ejnar Munksgaard, Copenhagen, 1955.

Since 1946, it has been possible for a woman in Sweden to obtain a "legal" abortion on various medical and social grounds, including psychiatric illness. The authors have followed up 479 cases in which the operation had been performed in 1949-50 in Stockholm. In some cases, the so-called "psychiatric" indication seems very vague and dubious, and the results of this conscientious survey of a sordid subject reveal some rather disturbing data.

One of the excuses for bringing in the Abortion Act in 1946 was the large number of illegal operations being performed in Sweden, but the Act appears not to have halted this unsavoury traffic but simply to have introduced a new clientele.

The excuse for terminating pregnancy that the woman had threatened suicide appears to be a poor one; the threat is seldom carried out.

At least 25% of the women admitted that they had guilt feelings about the operation; in 11% of cases the self-reproach and regret were serious.

Perhaps the best indication of the futility of the whole procedure is given by the fact that 37% of women had already gone through another pregnancy by the time of this survey, which clearly shows the grave responsibility placed on those recommending such measures.

THE TECHNIQUE OF PSYCHOANALYSIS

E. Glover. 404 pp. $6.00. Baillière, Tindall & Cox, London, England; The Macmillan Company of Canada Limited, Toronto, 1955.

There seems to be more fear of the reactions of the analyst than clear thinking about the relief to be afforded the psychotic in this volume. The text is full of the argot of psychoanalysis, but the reason for the use of it is not clear. No doubt the intimate relation between the patient and the patient analyst must produce some benefit to both. Insight into the ideas of another human being is difficult to arrive at, and the only effort at any special technique might be summed up in a few words. Perhaps, however, to listen, watch, ask questions and record the answers may be the only way to put the working of the individual mind under the microscope. The chapter on termination seemed to offer a little more concrete advice than any other.

CASIMIR FUNK

Pioneer in Vitamins and Hormones. B. Harrow, Professor Emeritus and Former Chairman of the Chemistry Department, The City College of New York. 209 pp. Illust. $3.00. Dodd, Mead & Company, New York, 1955.

Dr. Harrow has written exactly the type of biography that one might expect a distinguished biochemist to write about a colleague. He divides the biography of Casimir Funk into two parts—his life, and his work—and writes a plain account of both aspects of his hero's life with little attempt at dramatization.

In the first part he traces the career of this gifted biochemist, now over 70 years old, who is best known for his discovery of thiamine as the cause of beriberi, and for his coining of the word "vitamin," much against the wishes of his colleagues at the Lister Institute. Funk has been a wanderer all his life. From a childhood spent in Warsaw and a university career in Switzerland, he went on to work in Paris and then in Berlin under Emil Fischer and Abderhalden. He then transferred to London, where his important work on beriberi was done; in 1915 he moved on to New York and helped to pioneer the drug industry in the U.S.A., though his employer saw no future in vitamin preparations. After the war, he spent four years (1923-27) in Warsaw, where he worked on hormones, went back to Paris, where he worked on gonadotropins and sex hormones, and fled from France to New York in 1939. Latterly, he has been chiefly concerned with the biochemistry of cancer.

In the second part of the book Dr. Harrow faithfully records all the work that Funk has done, complete with publications.

For those who want to form a composite picture of Funk's activities, this book is ideal. Those seeking entertaining biography may be somewhat disappointed. Apart from one paragraph on page 108, Dr. Harrow gives us little insight into his subject's personality. This biography is more likely to be popular among biochemists than among the general public.

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Fluorine (as CaF_2)	0.1 mg.
Manganese (as MnO_2)	1 mg.
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Zinc (as ZnO)	0.5 mg.
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PERINATAL MORTALITY IN NEW YORK CITY

Responsible Factors. A Study of 955 Deaths by the Subcommittee on Neonatal Mortality, Committee on Public Health Relations, The New York Academy of Medicine, analysed and reported by S. G. Kohl, Associate Professor of Obstetrics and Gynecology, State University of the New York College of Medicine, New York. 112 pp. $2.75. The Harvard University Press, Cambridge, Massachusetts; S. J. Reginald Saunders and Co., Ltd., Toronto, 1955.

This study has already been commented on in our editorial columns (*Canad. M. A. J.*, 73: 406, 1955). It is an analysis of 955 perinatal deaths in New York City in 1950 and early 1951, made by a Subcommittee of the New York Academy of Medicine. This is an important piece of work, carefully carried out, and essential reading for all students of the subject. The project was designed to reveal the proportion of stillbirths and neonatal deaths which might have been prevented with better care. It is concluded that of the present series of deaths 35% were preventable. The great drawback in analysis is, as the authors admit, that no parallel series of surviving infants was studied. Further work is needed to include such a series and confirm whether some of the committee's conclusions are fully justified.

DISEASES TRANSMITTED FROM ANIMALS TO MAN

T. G. Hull, Secretary, Council on Scientific Assembly; Director, Bureau of Exhibits, American Medical Association. 717 pp. Illust. 4th ed. $13.75. Charles C Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1955.

This book is a mine of information on the common as well as the lesser known animal diseases communicable to man. Much inaccessible information has been gathered and presented in a form readable to physicians and others engaged in the practice of medicine. In a volume of 717 pages it is impossible to single out more than a few highlights for special comment. Among those of interest to the reviewer are an account of *Vibrio fœtus* abortion infection in cattle with a report of three human infections recorded in France. Likewise attention is drawn to the transmissibility of swine erysipelas to man through abraded skin with the causative organism *Erysipelothrix rhusiopathiæ*. The widespread occurrence of listerellosis in man in North America, Europe, Scotland, South America and Australia is described in an interesting chapter by Robert Graham.

The role of the apparently innocent skunk in the propagation of rabies is dealt with in a masterly article by Raymond A. Kelser. The fact that skunks may occasionally attack man is also recorded.

The chapter on avian Newcastle disease by C. M. Cunningham should be read by all physicians practising in rural districts as well as medical and ophthalmological specialists located in large cities. It reveals the widespread application of live virus vaccination in poultry husbandry and notes the recognition of human cases characterized by conjunctivitis, fever, chills, headache and general malaise.

It is unfortunate that only some three pages are devoted to the mysterious condition of benign lymphoreticulosis or cat scratch fever, of which much has been written in medical literature within recent years. Cat lovers may also be interested to note that the condition of hæmorrhagic septicæmia due to *Pasteurella multocida* infection may result from the bites of these feline beauties, according to Dr. Hull.

Passing from cats to rats, Wm. L. Jellison gives a succinct account of the etiology of rat bite fever also known as Haverhill fever, or erythema arthriticum epidemicum due to *Streptobacillus moniliformis* infection in man.

The reviewer was greatly impressed by the concluding chapter by Dr. Hull on the role of animals and birds in the transmission of disease to man. Sidelights on changing economic conditions affecting the animal population of the U.S.A. are contained in the statements that whereas in the year 1918 there were 21,555,000 horses on U.S. farms, only 4,763,000 remained in 1951. Simultaneously mules declined from 4,034,000 to 1,990,000 in the years between 1940 and 1951. In 1951 the number of cows in the U.S. is stated to be 84,170,000 and in 1950 the number of hogs was estimated at 56,964,000.

Limitation of space prevents fuller coverage of the contents of this excellent volume. The book is well printed and bound and strongly recommended for medical reading.

HOUSING THE AGING

Edited by W. Donahue. 280 pp. $3.75. The University of Michigan Press, Ann Arbor, Michigan, 1954.

This volume, the fifth in a series on the needs of the aging, is a Report of the Annual Conference on Aging, held at the University of Michigan, Ann Arbor, in July 1952. The conference was a joint project of the University of Michigan, the Michigan State Medical Society and certain federal agencies. The purpose of the conference was to review present knowledge regarding housing of older people, both the well and the ill, to promote interest in better housing for the aging, to assess the housing desires and needs of the older age groups, to study methods of financing this housing, and to encourage local governments to take a leading role in this planned programme of housing.

The contributors to this volume represent outstanding persons from many fields: the builder, the financier, the physician, the social worker, and the older people themselves.

Necessarily, most of the material refers to the United States and very brief reference is made to Canadian efforts in this field.

Since the whole "problem" of our aging population is, in part at least, iatrogenic in origin, it would be well for the Canadian physician, if he is truly interested in the total health of his patient, to be aware of the present-day problem of housing the aging population and the efforts that are being made toward its solution.

MEDICAL GREEK AND LATIN AT A GLANCE

W. R. Agard, Professor of Classics, University of Wisconsin, and H. M. Howe, Associate Professor of Classics, University of Wisconsin. 96 pp. 3rd ed. A Hoeber-Harper Book; Paul B. Hoeber, Inc., New York 16, 1955.

The amount of Latin and Greek known by medical students continues to diminish, and the need to interpret these languages to them correspondingly increases. The present work, which now appears in a third edition after a lapse of nearly twenty years, has little concern with the grammar of the two classical languages, but it is designed on strictly utilitarian lines. Its object is to present as rapidly and conveniently as possible a list of the most common Greek and Latin words related to medicine, with their English equivalents. Although it is designed for students at the premedical stage, many older students would benefit from consulting it, and many older practitioners would get quite a shock when they realized how little they know of the derivation of their technical terms. A portion of the book is devoted to exercises in etymology. The work can be recommended, though the need for it may be deplored.